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ARTICLE

An Evidence-Based Systematic Review of Goji (*Lycium* spp.) by the Natural Standard Research Collaboration

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ABSTRACT. An evidence-based systematic review of goji (*Lycium* spp.) by the Natural Standard Research Collaboration consolidates the safety and efficacy data available in the scientific literature using a validated, reproducible grading rationale. This article includes written and statistical analysis of clinical trials, plus a compilation of expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing.

KEYWORDS. Adverse effects, dosing, evidence-based, goji, interactions, *Lycium* spp., pharmacodynamics, pharmacokinetics, pharmacology, systematic review

SYSTEMATIC AGGREGATION, ANALYSIS, AND REVIEW OF THE LITERATURE

Search Strategy

To prepare this Natural Standard review, electronic searches were conducted in several databases (including AMED, CANCERLIT, CINAHL, CISCOP, the Cochrane Library, EMBASE, HerbMed, International Pharmaceutical Abstracts, Medline, and NAPRALERT) from inception to April 2013. Search terms included the common name(s), scientific name(s), and all listed synonyms. Hand searches were conducted of 20 additional journals (not indexed in common databases),

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and of bibliographies from 50 selected secondary references. No restrictions were placed on language or quality of publications. Researchers in the field of complementary and alternative medicine (CAM) were consulted for access to additional references or ongoing research.

Selection Criteria

All literature was collected pertaining to efficacy in humans (regardless of study design, quality, or language), dosing, precautions, adverse effects, use in pregnancy/lactation, interactions, alteration of laboratory assays, and mechanism of action (in vitro, animal research, human data). Standardized inclusion/exclusion criteria were utilized for selection.

Data Analysis

Data extraction and analysis were performed by healthcare professionals conducting clinical work and/or research at academic centers, using standardized instruments that pertained to each review section (defining inclusion/exclusion criteria and analytic techniques, including validated measures of study quality). Data were verified by a second reviewer.

Review Process

A blinded review was conducted by multidisciplinary research-clinical faculty at major academic centers with expertise in epidemiology and biostatistics, pharmacology, toxicology, complementary and alternative medicine (CAM) research, and clinical practice. In cases of editorial disagreement, a three-member panel of the Editorial Board addressed conflicts, and consulted experts when applicable. Authors of studies were contacted when clarification was required.

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Synonyms/Common Names/Related Substances

- Arabinogalactan proteins, ascorbic acid, atropine, Barbary wolfberry, betaine, beta-sitosterol, boxthorn, carotenoids, Chinese boxthorn, Chinese matrimony vine, Chinese wolfberry, cortex *Lycii radices*, Di Gu Pi, Digupi, dried wolfberries, fructus *Lycii*, fructus *Lycii* berry, fructus *Lycium barbarum* L., GoChi™, goji berry, goji juice, gou qi (Chinese), gou qi zi (Chinese), gouqi (Chinese), gouqizi (Chinese), Kei Tze, *L. exsertum*, *L. fremontii*, Lacto-Wolfberry, lutein, *Lycii* berries, *Lycii chinensis*, *Lycii fructus*, *Lycii fruit*, *Lycium*, *Lycium barbarum*, *Lycium barbarum* L., *Lycium barbarum* polysaccharides (LBP), *Lycium californicum*, *Lycium chiense*, *Lycium chinense*, *Lycium chinense* Miller, *Lycium europeum*, *Lycium halimifolium* Mill., *Lycium nodosum*, *Lycium parishii*, *Lycium ruthenicum*, *Lycium shawii*, *Lycium vulgare* Dunal, matrimony vine, Ning Xia Gou Qi (Chinese), polysaccharides, scopoletin, Solanaceae (family), Tibetan goji berry, vitamin C, wolfberry, wolfberry fruit, zeaxanthin.
- **Select combination products:** Runmushu oral liquid (rehmannia root, figwort, lilyturf root, dendrobium stem, wolfberry fruit, chrysanthemum, and sticktight).

CLINICAL BOTTOM LINE/EFFECTIVENESS

Brief Background

- According to secondary sources, the origins of goji berries (*Lycium barbarum* and *Lycium chinense*) are lost in antiquity. They have been consumed as a food and as medicine in Asia for at least 2,000 years (Adams, Wiedenmann, Tittel, & Bauer, 2006; Yu, Ho, So, Yuen, & Chang, 2006). The common name, “wolfberry,” is often used in the scientific literature. There is some controversy as to whether goji is indeed synonymous with wolfberry, and most experts agree that they are similar, but not identical, because they are grown in different parts of Asia. However, the health-food industry has adopted the name “goji,” which is a simplified pronunciation of the Mandarin name *gouqi*.
- The leaves, roots, and root bark of *Lycium* species have also been used medicinally. Traditionally, goji berries have been used to support the kidneys and the liver, to protect the eyes, to enhance the immune system, and to treat male infertility, as well as an antiaging tonic (Luo et al., 2006; Tierra, 1988; Yu et al., 2005, 2006). Goji berries are nutrient rich and contain significant quantities of the carotenoids lutein and zeaxanthin, which provides a logical rationale for their antiaging and visual protection applications (Benzie, Chung, Wang, Richelle, & Bucheli, 2006; Breithaupt, Weller, Wolters, & Hahn, 2004; Gribanovski-Sassu, Pellicciari, & Cataldi Hiughez, 1969; Kim, Kim, Lee, Kim, & Kim, 1997b; Peng et al., 2005; Weller & Breithaupt, 2003). A valid topic for further investigation is the potential of goji berry consumption to prevent macular degeneration.
- Although adequate human clinical data on the efficacy of goji berry preparations are lacking, there is a significant and growing body of in vitro and animal research. A significant portion of this research focuses on the physiological effects of *Lycium barbarum* polysaccharides (LBP). Various polysaccharide components extracted from goji berries have already demonstrated anticancer, antidiabetes, antihypertensive, antiinfertility, antimyelosuppressive, antioxidant, hypolipidemic, immune-stimulating, and radiosensitizing properties (Gan, Hua Zhang, Liang Yang, & Bi Xu, 2004; Gan, Wang, & Zhang, 2001; Gong, Shen, Jin, Xing, & Tang, 2005; He et al., 2005; Huang, Tian, Wang, Dong, & Wu, 2001; Jia, Dong, Wu, Ma, & Shi, 1998; Lu & Cheng, 1991; Luo, Cai, Yan, Sun, & Corke, 2004; Luo, Yan, & Zhang, 1999; Wang et al., 2002; Wu, Guo, & Zhao, 2006; Zhang, Zhang, & Li, 1997; Zhang et al., 2005; Zhao, Li, & Xiao, 2005). Therefore, investigations utilizing *Lycium* polysaccharides should be a fruitful area for clinical research.

Scientific Evidence

Asthma	C
Cancer	C
Cognition	C
Immunomodulation	C
Skin aging	C
Vision	C
Weight loss/obesity	C
Well-being	C

Natural Standard Evidence-Based Validated Grading RationaleTM

- Grades reflect the level of available scientific evidence in support of the efficacy of a given therapy for a specific indication.
- Expert opinion and historic/folkloric precedent are not included in this assessment, and are reflected in a separate section of each review (“Expert Opinion and Historic/Folkloric Precedent”).
- Evidence of harm is considered separately; the below grades apply only to evidence of benefit.

Level of evidence grade	Criteria
A (strong scientific evidence)	Statistically significant evidence of benefit from >2 properly randomized trials (RCTs), OR evidence from one properly conducted RCT AND one properly conducted meta-analysis, OR evidence from multiple RCTs with a clear majority of the properly conducted trials showing statistically significant evidence of benefit AND with supporting evidence in basic science, animal studies, or theory.
B (good scientific evidence)	Statistically significant evidence of benefit from 1–2 properly randomized trials, OR evidence of benefit from >1 properly conducted meta-analysis OR evidence of benefit from >1 cohort/case-control/non-randomized trials AND with supporting evidence in basic science, animal studies, or theory.
C (unclear or conflicting scientific evidence)	Evidence of benefit from >1 small RCT(s) without adequate size, power, statistical significance, or quality of design by objective criteria,* OR conflicting evidence from multiple RCTs without a clear majority of the properly conducted trials showing evidence of benefit or ineffectiveness, OR evidence of benefit from >1 cohort/case-control/non-randomized trials AND without supporting evidence in basic science, animal studies, or theory, OR evidence of efficacy only from basic science, animal studies, or theory.
D (fair negative scientific evidence)	Statistically significant negative evidence (i.e., lack of evidence of benefit) from cohort/case-control/non-randomized trials, AND evidence in basic science, animal studies, or theory suggesting a lack of benefit.
F (strong negative scientific evidence)	Statistically significant negative evidence (i.e. lack of evidence of benefit) from >1 properly randomized adequately powered trial(s) of high-quality design by objective criteria.*
Lack of evidence†	Unable to evaluate efficacy due to lack of adequate available human data.

*Objective criteria are derived from validated instruments for evaluating study quality, including the 5-point scale developed by Jadad et al., in which a score below 4 is considered to indicate lesser quality methodologically (Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Controlled Clinical Trials* 1996; 17[1]:1–12).

†Listed separately in the “Historical or Theoretical Uses That Lack Sufficient Evidence” section.

Historical or Theoretical Uses That Lack Sufficient Evidence

- Acne, aging (Chan et al., 2007; Deng et al., 2003; Ho, So, & Chang, 2010; Wu, Zou, & Meng, 2003; Yu et al., 2005, 2006), alcohol abuse, Alzheimer’s disease (Yu et al., 2005), anemia (Hai-Yang, Ping, Li, Chang-Hong, & Fu, 2004), antifungal (Lee et al., 2004), antiinflammatory (Wei et al., 2002), antimicrobial (Lee, Jung, & Woo, 2005), antioxidant (Han, Lee, Lee, Moon, & Woo, 2002; Huang et al., 2001; Huang, Yang, Wu, & Yan, 2003; Huang, Lu, Shen, & Lu, 1999; Huang, Tan, Shen, & Lu, 1998; Kim et al., 2002; Li, Qu, Zhang, & Lv, 2006; Li, Yang, Ren, & Wang, 2002; Lu, 2005; Luo et al., 2004; Ni, Qing, Kaisa, & Lu, 2004; Peng,

Wang, & Tian, 2001; Ren, Ma, Shen, & Gao, 1995; Wu et al., 2006; Wu, Ng, & Lin, 2004; Zhang, 1993), arthritis, atherosclerosis (Potterat, 2010), athletic performance (Amagase & Nance, 2008; Amagase & Nance, 2011), attention-deficit hyperactivity disorder, autism, bowel health (Amagase & Nance, 2008), chemotherapy adverse effects (Gong et al., 2005), chronic fatigue syndrome, cough, depression, diabetes (Lu, 2005; Luo et al., 2004; Shabana, Mirhom, Genenah, Aboutabl, & Amer, 1990; Wu et al., 2006; Zhao et al., 2005), dizziness, fatigue (Amagase & Nance, 2008; Luo, Yan, & Zhang, 2000), fever, food uses (Adams et al., 2006; Lin, Chiu, & Pan, 2004; Pieroni, Nebel, Quave, Munz, & Heinrich, 2002), gastrointestinal reflux disease (acid reflux), heart muscle injury (Xu, Huang, & Tian, 2005), hypertension (Jia et al., 1998), improving circulation, infertility (Luo et al., 2006; Suzuki, Osawa, & Hirano, 1972; Wang et al., 2002), irritability, kidney protection (Yu et al., 2006), lipid lowering effects (Luo et al., 2004), liver protection (Chin et al., 2003; Ha et al., 2005; Kim et al., 1997a; 1997b; Ram, 2001; Yu et al., 2006), low blood platelets (Hai-Yang et al., 2004), muscle strength, neuroprotection (Lin, Hou, Yen, & Lee, 2003; Meng et al., 2007; Yu et al., 2005, 2006), nosebleeds, oral hygiene (Hiserodt, Adedeji, John, & Dewis, 2004), osteoporosis (Yin et al., 2004), periodontal disease (Liu, 1992), radioprotection (Hsu, Yang, Ho, & Lin, 1999; Lu & Cheng, 1991), respiratory disease (Lee et al., 2004), restless legs syndrome, stress (Amagase & Nance, 2008), sweating, thirst, tinnitus, tonic.

Expert Opinion and Historic/Folkloric Precedent

- According to secondary sources, the dried ripe fruits of *Lycium barbarum* L. and *Lycium chinense*, commonly called goji berry or wolfberry, have been consumed for at least 2,000 years in China and throughout Asia for medicinal purposes and as a functional food. Goji is a 1–2 cm-long, bright orange-red, ellipsoid berry. Traditionally, goji berry has been used for its antiaging properties; for its beneficial effects on vision, the immune system, the kidneys, and the liver; and as a treatment for respiratory diseases (Adams et al., 2006; Du, Wang, Huang, Li, & Shao, 1994; Hai-Yang et al., 2004; Lee et al., 2004; Yu et al., 2006). *Lycium barbarum* fruits are also used by Chinese physicians to treat infertility in men (Luo et al., 2006; Wang et al., 2002).
- Scientists are investigating the mechanisms of action underlying the physiological properties of goji. Recent research has shown that *Lycium barbarum* extracts demonstrate antiaging, anticancer, immune-stimulating, and cytoprotective activity. Many of these protective functions may be due to its antioxidant effects (Yu et al., 2006). Other scientists have investigated the immune-modulating (Du, Liu, & Fang, 2004; Duan et al., 2001; Gan et al., 2004; Gan, Zhang, Liu, & Xu, 2003; He et al., 2005; Huang, Lin, Tian, & Ji, 1998; Huang, Tian, & Ji, 1999; Lu, 2005; Luo et al., 1999; Peng & Tian, 2001; Peng et al., 2001; Tang et al., 2012; Yu et al., 2006) and antitumor (Gan et al., 2004; He et al., 2005; Tang et al., 2012; Yu et al., 2006) effects of goji. General reviews on goji have also been written (Potterat, 2010).
- Approximately 70 species of *Lycium* grow in separate and distinct regions distributed in temperate to subtropical parts of North America, South America,

southern Africa, Eurasia, and Australia (Fukuda, Yokoyama, & Ohashi, 2001). Ethnobotanists have found that *Lycium* is still used by healers in Israel (Dafni & Yaniv, 1994). In recent years, goji berry and juice products have become increasingly popular in the United States. However, goji is not on the U.S. Food and Drug Administration (FDA) Generally Recognized as Safe (GRAS) list.

Brief Safety Summary

- **Possibly unsafe:** When used in patients with bleeding disorders or those who are taking blood-thinning medications, such as warfarin, according to case reports of elevated international normalized ratios (INR) (Lam, Elmer, & Mohutsky, 2001; Leung, Hung, Hui, & Chan, 2008; Rivera, Ferro, Bursua, & Gerber, 2012). When used in patients with diabetes or hypoglycemia and those taking drugs, herbs, or supplements that affect blood sugar, based on animal research reporting decreased blood sugar (Luo et al., 2004; Shabana et al., 1990; Wu et al., 2006; Zhao et al., 2005). When used in patients with low blood pressure or in those taking drugs, herbs, or supplements that lower blood pressure, based on animal research reporting decreased blood pressure (Jia et al., 1998). When used in patients undergoing radiation therapy as in animal research, a combination of *Lycium barbarum* polysaccharide and radiation had significant radiosensitizing effects (Lu & Cheng, 1991). When used in pregnant or breastfeeding women, as, according to anecdotal reports, goji may stimulate the uterus. When used in patients with skin conditions, based on a case report of a 53 year-old man presenting with a pruriginous eruption on sun-exposed areas of the skin related to goji consumption (Gomez-Bernal et al., 2011). When used in individuals with gastrointestinal conditions, based on a case report of autoimmune hepatitis triggered by consumption of goji berries (further details lacking) (Franco, Monmany, Domingo, & Turbau, 2012), and according to anecdotal reports, high doses of goji berry extract may cause nausea and vomiting. When used in patients with allergies to peach, tomatoes, tobacco, and nuts, based on tests in humans indicating cross-reactivity between goji and those items (Carnes et al., 2013; Larramendi et al., 2012; Monzon Ballarin, Lopez-Matas, Saenz Abad, Perez-Cinto, & Carnes, 2011). Both cases tested positively to a goji skin prick test and IgE to goji. Again, LTPs were implicated as likely, and cross-reactivity to tomatoes was suggested.
- **Likely unsafe:** When used in asthma patients and in patients with sulfite sensitivities, as the New York Department of Agriculture detected the presence of undeclared sulfites, a food additive, in two dried goji berry products from China. When used in patients who are allergic to *Lycium barbarum* L. berries, root bark, roots, leaves, any of its constituents, or to members of the Solanaceae family.

DOSING/TOXICOLOGY

General

- Doses may be based on those most commonly used in available trials, or on historical practice. However, with natural products it is often not clear what the

optimal doses are to balance efficacy and safety. Preparation of products may vary from manufacturer to manufacturer, and from batch to batch within one manufacturer. Because it is often not clear what the active component(s) of a product is, standardization may not be possible, and the clinical effects of different brands may not be comparable.

Standardization

- A well-known standardization for goji is lacking.
- According to the author of a clinical trial of a goji fruit juice, the *L. barbarum* fruit juice (GoChi™, FreeLife International Inc., Phoenix, AZ) was prepared from *L. barbarum* fruit, the yield from the fresh plant was approximately 35%, and the juice contained *L. barbarum* polysaccharides that were equivalent to those found in 150 g of fresh fruit (Amagase & Nance, 2008, 2011; Amagase, Sun, and Nance, 2009).
- In a clinical trial, each gram of Lacto-Wolfberry product contained 530 mg of wolfberry fruit, 290 mg of bovine skimmed milk, and 180 mg of maltodextrin (Vidal et al., 2012).

Dosing

Adult (age ≥18)

Oral.

- **General:** According to an herbal text, 6–15 g daily of *Lycium* berries is commonly used (Tierra, 1988). According to anecdotal reports, 3–4 oz. of goji juice has been taken for a variety of conditions. Traditionally, *Lycium* has been taken as a tea. A typical dose is one or more cups of tea daily, but the strength of the tea is based on the condition being treated.
- **Cognition:** 120 ml of *L. barbarum* juice (GoChi™, FreeLife International, Phoenix, AZ) has been taken daily for 30 days (Amagase et al., 2009).
- **Immunomodulation:** 120 ml of *L. barbarum* juice (GoChi™, FreeLife International, Phoenix, AZ) has been taken daily for 30 days (Amagase et al., 2009).
- **Vision:** 120 ml of *L. barbarum* juice (GoChi™, FreeLife International, Phoenix, AZ) has been taken daily for 30 days (Amagase et al., 2009).
- **Weight loss/obesity:** 120 ml of *L. barbarum* juice has been taken daily (90 ml at breakfast and 30 ml at bedtime) for 14 days (exercise and caloric restriction was also followed) (Amagase & Nance, 2011).
- **Well-being:** According to a meta-analysis, in all included studies, participants consumed 120 ml of *L. barbarum* juice (GoChi™, FreeLife International, Phoenix, AZ) daily for 14–30 days (Amagase & Nance, 2008; Amagase et al., 2009; Paul Hsu, Nance, & Amagase, 2012).

Children (age <18)

- Insufficient available evidence.

Toxicology

- Toxic effects were lacking in some available clinical trials (Amagase et al., 2009; Vidal et al., 2012).
- There have been reports of the presence of atropine in Barbary wolfberries (goji berries) from India (Adams et al., 2006). Since the dried ripe fruits of Barbary wolfberry, *Lycium barbarum* L., are extensively used as a functional food and medicine in China, there has been concern about whether the berries are suitable for human consumption. Researchers therefore, analyzed eight samples of berries from China and Thailand for traces of atropine. After they utilized highly selective and sensitive HPLC-MS methods, atropine was found in all examined samples in concentrations of maximally 19ppb (w/w). The investigators concluded that the content of atropine in dried ripe berries of *Lycium barbarum* L. is far below toxic levels.
- Little toxicity was observed with administration of *Lycium barbarum* polysaccharide (LBP) to Lewis lung cancer cell transplanted C57 BL mice (Lu & Cheng, 1991).
- According to secondary sources, the U.S. Food and Drug Administration (FDA) detected high levels of pyrethroid insecticide residues and fungicide residues in goji berries and goji products imported from China, leading to seizure of these products.
- An anaphylactic reaction to goji berries has been reported in a case report (Monzon Ballarin et al., 2011). There is a report of autoimmune hepatitis triggered by consumption of goji berries (further details are lacking) (Franco et al., 2012)
- Although further details are lacking, *Lycium barbarum* was described as a new hepatotoxic “natural” agent in a letter (Arroyo-Martinez, Saenz, Arguelles Arias, & Acosta, 2011).

ADVERSE EFFECTS/PRECAUTIONS/CONTRAINDICATIONS

Allergy

- Avoid with known allergy or hypersensitivity to *Lycium barbarum* L. berries, root bark, roots, leaves, their constituents, or members of the Solanaceae family.
- Avoid with known allergy or hypersensitivity to sulfites. In 2006 and 2007, the New York State Department of Agriculture detected the presence of undeclared sulfites in two separate dried goji berry products. The agriculture commissioner warned sulfite-sensitive consumers and asthmatics to avoid consumption of these products. Sulfites do not occur naturally in goji berries. They are a preservative that is commonly used in dried fruits and vegetables. When added to foods, sulfites must be declared on the label.
- Of 566 individuals with respiratory or cutaneous symptoms, skin prick tests with goji berries revealed that 33 (5.8%) were positive, and 92.3% of the patients that tested positive to goji berries also tested positive to peach (Carnes et al., 2013). Cross-reactivity was demonstrated with tomato, tobacco, and a nut mix, as well as with two purified proteins, Lyc e 3 and Pru p 3. The major allergen was suggested

to be panallergen nonspecific lipid transfer protein (LTP). Of 30 patients with food allergies, 20 of whom had never tried goji berries previously, six who had tried and tolerated the berries, and four who had tried and reported symptoms on intake, skin tests to goji were positive in 24 (Larramendi et al., 2012). Of the 24, 19 were asymptomatic and 5 were symptomatic. The authors determined that a skin test positive to goji was associated with a skin test positive to peach peel, as well as to LTP. IgE to goji was detected.

- In a separate publication, the authors reported to cases of goji allergy, one resulting in an anaphylactic reaction (Monzon Ballarin et al., 2011). Both cases tested positively to a goji skin prick test and IgE to goji. Again, LTPs were implicated as likely, and cross-reactivity to tomatoes was suggested.

Adverse Effects

- **General:** There is a lack of available information on the adverse effects of goji. According to anecdotal reports, high doses of goji berry extract may induce alertness at bedtime and may interfere with sleep. According to secondary sources, goji may also cause nausea and vomiting. Case reports have demonstrated the occurrence of a pruriginous eruption on sun-exposed areas of the skin (Gomez-Bernal et al., 2011) and autoimmune hepatitis (Franco et al., 2012). Adverse effects were lacking in some available clinical trials (Amagase & Nance, 2008; Amagase et al., 2009).
- **Dermatologic:** In a case report, a 53-year-old man presented with a pruriginous eruption on sun-exposed areas of the skin (Gomez-Bernal et al., 2011). The eruption had lasted for two weeks. Upon testing, it was revealed that the patient tested positive to goji berries in a photoprovocation test, but not to cat's claw (which he was also taking at the same time).
- **Gastrointestinal:** There is a report of autoimmune hepatitis triggered by consumption of goji berries (further details are lacking) (Franco et al., 2012). According to anecdotal reports, high doses of goji berry extract may cause nausea and vomiting. In a clinical trial, vomiting occurred in the Lacto-Wolfberry group (Vidal et al., 2012).
- **Other:** In a clinical trial, fever occurred in the Lacto-Wolfberry group (Vidal et al., 2012).

Precautions/Warnings/Contraindications

- Use cautiously in patients with bleeding disorders or those who are taking blood-thinning medications, such as warfarin, based on case reports of elevated international normalized ratios (INR) (Lam et al., 2001; Leung et al., 2008; Rivera, Ferro, Bursua, & Gerber, 2012).
- Use cautiously in patients with diabetes or hypoglycemia and those taking drugs, herbs, or supplements that affect blood sugar, based on animal research reporting decreased blood sugar (Luo et al., 2004; Shabana et al., 1990; Wu et al., 2006; Zhao et al., 2005).
- Use cautiously in patients with low blood pressure or those taking drugs, herbs, or supplements that lower blood pressure, based on animal research reporting decreased blood pressure (Jia et al., 1998). However, in human research, GoChi™

lacked a statistically significant effect on systolic and diastolic blood pressure (Amagase & Nance, 2008).

- Use cautiously in patients undergoing radiation therapy as, in animal research, a combination of *Lycium barbarum* polysaccharide and radiation had significant radiosensitizing effects (Lu & Cheng, 1991).
- Use cautiously in pregnant or breastfeeding women, as, according to anecdotal reports, goji may stimulate the uterus.
- Use cautiously in patients with skin conditions, based on a case report of a 53-year-old man presenting with a pruriginous eruption on sun-exposed areas of the skin related to goji consumption (Gomez-Bernal et al., 2011).
- Use cautiously in individuals with gastrointestinal conditions, based on a case report of autoimmune hepatitis triggered by consumption of goji berries (further details are lacking) (Franco et al., 2012), and according to anecdotal reports, high doses of goji berry extract may cause nausea and vomiting.
- Use cautiously in patients with allergies to peach, tomatoes, tobacco, and nuts, based on tests in humans indicating cross-reactivity between goji and those items (Carnes et al., 2013; Larramendi et al., 2012; Monzon Ballarin et al., 2011). Both cases tested positively to a goji skin prick test and IgE to goji. Again LTPs were implicated as likely, and cross-reactivity to tomatoes was suggested.
- Avoid in asthma patients and patients with sulfite sensitivities. The New York Department of Agriculture detected the presence of undeclared sulfites, a food additive, in two dried goji berry products from China.
- Avoid in those with allergy or hypersensitivity to *Lycium barbarum* L. berries, root bark, roots, leaves, their constituents, members of the Solanaceae family.

Pregnancy and Lactation

- According to anecdotal reports, *Lycium* may have uterine stimulant properties.
- Information on goji's effects on lactation is lacking in the National Institute of Health's Lactation and Toxicology Database (LactMed).
- **Animal data:** Researchers systematically investigated the effect of *L. barbarum* polysaccharides (LBP) on male infertility in a rat model of testis damage induced by a physical factor (43°C heat exposure), on DNA damage of mouse testicular cells induced by a chemical factor (H₂O₂), and on sexual behavior and reproductive function of hemicastrated male rats (Luo et al., 2006). The results showed that LBP had a positive and protective effect on all studied parameters, including a protective effect against the testicular tissue damage induced by heat exposure, a significant increase in testis and epididymis weights, improved superoxide dismutase (SOD) activity, and raised sexual hormone levels in the damaged rat testes. LBP also protected against DNA oxidative damage of mouse testicular cells induced by H₂O₂ in a dose-dependent manner. In hemicastrated male rats, LBP improved the copulatory performance and reproductive function, such as shortened penis erection latency and mount latency, regulated secretion of sexual hormones, increased hormone levels, raised accessory sexual organ weights, and improved sperm quantity and quality. These results provide scientific evidence to support the traditional use of *Lycium barbarum* fruits as an aphrodisiac and a traditional remedy for male infertility in China.

- Fructus *Lycii*, the fruits of *Lycium barbarum* L. (Solanaceae), are used by Chinese physicians for the treatment of infertility (Wang et al., 2002). An in vitro research study demonstrated that fructus *Lycii* polysaccharides (FLPS) inhibit hyperthermia- and time-induced structural damage in mouse seminiferous epithelium. Furthermore, FLPS delayed apoptosis in this system, both at normothermic and hyperthermic culture conditions. FLPS was found to be a potent inhibitor of both ultraviolet light-induced lipid peroxidation and cytochrome c reduction by free radicals. Since it has been reported that oxidative stress is a major cause of structural damage and apoptosis in hyperthermic testes, the authors proposed that the protective effect of FLPS on time- and hyperthermia-induced testicular degeneration in vitro is due to its antioxidant properties.
- When fed to weanling mice, *Lycium barbarum* polysaccharides (LBP-4) enhanced the content of zinc and iron in pygal muscles and femora, and reduced body weight (Zhang, Wang, & Zhang, 2002).

INTERACTIONS

Goji/Drug Interactions

- **Antibiotics:** In vitro, the root bark from *Lycium chinense* Miller had antimicrobial activity against antibiotic-resistant bacterial strains, methicillin-resistant *Staphylococcus aureus* (MRSA), and human pathogenic fungi (Lee et al., 2005).
- **Anticoagulants and antiplatelets:** In case reports of individuals stabilized on warfarin, *Lycium barbarum* L. fruit elevated the international normalized ratio (INR) (Lam et al., 2001; Leung et al., 2008). A patient on warfarin presented to the hospital with an elevated INR, as well as symptoms of epistaxis, bruising, and rectal bleeding (Rivera, Ferro, Bursua, & Gerber, 2012). The patient had recently consumed goji juice for four days, with no other dietary changes. The patient was treated with phytonadione, and goji juice and warfarin were discontinued, resulting in a decrease in the INR over two days.
- **Antidepressants, MAOIs:** In vitro, *Lycium chinense* inhibited MAO-B (Lin et al., 2003).
- **Antidiabetics:** In animal research, *Lycium barbarum* decreased plasma glucose and 30-min postprandial glucose levels (Luo et al., 2004; Shabana et al., 1990; Wu et al., 2006; Zhao et al., 2005).
- **Antifungals:** In vitro, an ethyl acetate extract of the root bark of *Lycium chinense* Miller had an antifungal effect (Lee et al., 2005; Lee et al., 2004).
- **Antihypertensives:** In animal research, *Lycium* constituents had antihypertensive effects (Jia et al., 1998). However, in human research, GoChi™ lacked a statistically significant effect on systolic and diastolic blood pressure (Amagase & Nance, 2008).
- **Antilipemics:** In animal research, *Lycium barbarum* decreased plasma cholesterol and plasma triglycerides (Luo et al., 2004; Zhao et al., 2005).

- **Antineoplastics:** In vitro and in animal research, *Lycium barbarum* had antineoplastic effects (Chao, Chiang, Wang, Tsai, & Wu, 2006; Gan et al., 2001, 2004; Gong et al., 2005; Hai-Yang et al., 2004; Liu, Sun, Li, Zhang, & Qian, 2000; Miao et al., 2010; Stoner et al., 2010; Zhang et al., 2005).
- **Antivirals:** In vitro, *Lycium* fruit had antiviral activity (Wang, Jiang, & Chen, 1991).
- **Cardiovascular agents:** In vitro, *Lycium barbarum* had cardioprotective activity (Xu et al., 2005).
- **Cognitive improvement agents:** In human research, GoChi™ improved mental acuity (Paul Hsu et al., 2012).
- **Cytochrome P450-modifying agents:** In vitro, a tea of *L. barbarum* L. weakly inhibited S-warfarin metabolism by CYP2C9 (Lam et al., 2001).
- **Dermatologic agents:** In a case report, it was determined that goji was responsible for a pruriginous eruption on sun-exposed areas of the skin (Gomez-Bernal et al., 2011). In vitro, a combination of Himalayan actives including goji berries attenuated ultraviolet B (UVB)-induced cell apoptosis of skin organ epidermis and decreased TNF-alpha secretion (Wineman et al., 2012). In human research, topical application reduced wrinkle depth (Wineman et al., 2012).
- **Exercise agents:** In human research, *L. barbarum* increased VO₂ (Amagase & Nance, 2011).
- **Hepatotoxins:** In animal research, *Lycium chinense* Miller (Solanaceae) had hepatoprotective effects and decreased levels of serum aspartate and alanine aminotransferase (AST and ALT) and alkaline phosphatase (ALP) (Ha et al., 2005).
- **Hormonal agents:** In vitro, *Lycium barbarum* regulated and increased the secretion of male sexual hormones (Luo et al., 2006).
- **Immunosuppressants:** In human research, results from available randomized controlled trials suggested that wolfberry alters immune response, such as enhancing the capacity to respond to antigenic challenge (Vidal et al., 2012) and increasing the number of lymphocytes and levels of interleukin-2 and immunoglobulin G (Amagase et al., 2009; Vidal et al., 2012). In animal research, *Lycium* had immunostimulatory activity (Gan et al., 2004; He et al., 2005; Lin, Lu, Liou, & Liou, 2006).
- **Insulin preparations:** In animal research, *Lycium barbarum* significantly increased insulin sensitivity (Zhao et al., 2005).
- **Interleukins:** In patients with advanced cancer, *Lycium barbarum* polysaccharides administered in conjunction with LAK/IL-2 increased NK and LAK cell activity (Cao, Yang, & Du, 1994).
- **Mood stabilizers:** In human research, GoChi™ improved calmness and depression (Paul Hsu et al., 2012).
- **Ophthalmic agents:** In human research, a combination product containing goji was found to improve xerophthalmia in postmenopausal women (Wei, Li, & Zhou, 2009). In human research, Lacto-Wolfberry (a proprietary milk-based formulation of goji) prevented effects on pigmentation and soft drusen count in the macula in elderly subjects (Bucheli et al., 2011). In human research, GoChi™ lacked a statistically significant effect on eye fatigue or vision (Amagase & Nance, 2008).

- **Osteoporosis agents:** In laboratory research, a water extract of *Lycium chinense* stimulated osteoblast proliferation and inhibited osteoclast formation (Yin et al., 2004).
- **Respiratory agents:** In human research, GoChi™ improved shortness of breath (Paul Hsu et al., 2012)
- **Sedatives:** In human research, GoChi™ improved the ease of awakening and sleep quality, as well as fatigue (Amagase & Nance, 2008; Paul Hsu et al., 2012).
- **Weight loss agents:** In a clinical trial of GoChi™ fruit juice, the juice resulted in an increased reduction in waist circumference, but not a reduction in body weight, in subjects that were also exercising (Amagase & Nance, 2011). In human research, GoChi™ lacked a statistically significant effect on body weight, body mass index (BMI), and body fat (Amagase & Nance, 2008).

Goji/Herb/Supplement Interactions

- **Antibacterials:** In vitro, the root bark from *Lycium chinense* Miller had antimicrobial activity against antibiotic-resistant bacterial strains, methicillin-resistant *Staphylococcus aureus* (MRSA), and human pathogenic fungi (Lee et al., 2005).
- **Anticoagulants and antiplatelets:** In case reports of individuals stabilized on warfarin, *Lycium barbarum* L. fruit elevated the international normalized ratio (INR) (Lam et al., 2001; Leung et al., 2008). A patient on warfarin presented to the hospital with an elevated INR, as well as symptoms of epistaxis, bruising, and rectal bleeding (Rivera, Ferro, Bursua, & Gerber, 2012). The patient had recently consumed goji juice for four days, with no other dietary changes. The patient was treated with phytonadione, and goji juice and warfarin were discontinued, resulting in a decrease in the INR over two days.
- **Antidepressants: MAOIs:** In vitro, *Lycium chinense* inhibited MAO-B (Lin et al., 2003).
- **Antifungals:** In vitro, an ethyl acetate extract of the root bark of *Lycium chinense* Miller had an antifungal effect (Lee et al., 2004, 2005).
- **Antilipemics:** In animal research, *Lycium barbarum* decreased plasma cholesterol and plasma triglycerides (Luo et al., 2004; Zhao et al., 2005).
- **Antineoplastics:** In vitro and in animal research, *Lycium barbarum* had antineoplastic effects (Chao et al., 2006; Gan et al., 2001, 2004; Gong et al., 2005; Hai-Yang et al., 2004; Liu et al., 2000; Miao et al., 2010; Stoner et al., 2010; Zhang et al., 2005).
- **Antioxidants:** In human research, goji increased levels of superoxide dismutase (SOD) and glutathione peroxidase, and decreased levels of malondialdehyde (MDA) (Amagase, Sun, & Borek, 2009). In human research, Lacto-Wolfberry (a proprietary milk-based formulation of goji) increased plasma zeaxanthin levels and the antioxidant capacity (Bucheli et al., 2011). In animal research, wolfberry resulted in an increase in serum antioxidant activity (Stoner et al., 2010).
- **Antivirals:** In vitro, *Lycium* fruit had antiviral activity (Wang et al., 1991).
- **Cardiovascular agents:** In vitro, *Lycium barbarum* had cardioprotective activity (Xu et al., 2005).
- **Cognitive improvement agents:** In human research, GoChi™ improved mental acuity (Paul Hsu et al., 2012).

- **Cytochrome P450-modifying agents:** In vitro, a tea of *L. barbarum* L. weakly inhibited S-warfarin metabolism by CYP2C9 (Lam et al., 2001).
- **Dermatologic agents:** In a case report, it was determined that goji was responsible for a pruriginous eruption on sun-exposed areas of the skin (Gomez-Bernal et al., 2011). In vitro, a combination of Himalayan actives including goji berries attenuated UVB-induced cell apoptosis of skin organ epidermis and decreased TNF-alpha secretion (Wineman et al., 2012). In human research, topical application reduced wrinkle depth (Wineman et al., 2012).
- **Exercise agents:** In human research, *L. barbarum* increased VO_2 (Amagase & Nance, 2011).
- **Hepatotoxic herbs:** In animal research, *Lycium chinense* Miller (Solanaceae) had hepatoprotective effects and decreased levels of serum aspartate and alanine aminotransferase (AST and ALT) and alkaline phosphatase (ALP) (Ha et al., 2005).
- **Hormonal herbs and supplements:** In vitro, *Lycium barbarum* regulated and increased the secretion of male sexual hormones (Luo et al., 2006).
- **Hypoglycemics:** In animal research, *Lycium barbarum* decreased plasma glucose and 30-min postprandial glucose levels (Luo et al., 2004; Shabana et al., 1990; Wu et al., 2006; Zhao et al., 2005).
- **Hypotensives:** In animal research, *Lycium* constituents had antihypertensive effects (Jia et al., 1998). However, in human research, GoChi™ lacked a statistically significant effect on systolic and diastolic blood pressure (Amagase & Nance, 2008).
- **Immunostimulants:** In human research, results from available randomized controlled trials suggested that wolfberry alters immune response, such as enhancing the capacity to respond to antigenic challenge (Vidal et al., 2012) and increasing the number of lymphocytes and levels of interleukin-2 and immunoglobulin G (Amagase et al., 2009; Vidal et al., 2012). In animal research, *Lycium* had immunostimulatory activity (Gan et al., 2004; He et al., 2005; Lin et al., 2006).
- **Iron:** In animal research, *Lycium barbarum* polysaccharides (LBP-4) increased the level of iron in muscle and bone (Zhang et al., 2002).
- **Mood stabilizers:** In human research, GoChi™ improved calmness and depression (Paul Hsu et al., 2012).
- **Ophthalmic agents:** In human research, a combination product containing goji was found to improve xerophthalmia in postmenopausal women (Wei et al., 2009). In human research, Lacto-Wolfberry (a proprietary milk-based formulation of goji) prevented effects on pigmentation and soft drusen count in the macula in elderly subjects (Bucheli et al., 2011). In human research, GoChi™ lacked a statistically significant effect on eye fatigue or vision (Amagase & Nance, 2008).
- **Osteoporosis agents:** In laboratory research, a water extract of *Lycium chinense* stimulated osteoblast proliferation and inhibited osteoclast formation (Yin et al., 2004).
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- **Sedatives:** In human research, GoChi™ improved the ease of awakening and sleep quality, as well as fatigue (Amagase & Nance, 2008; Paul Hsu et al., 2012).

- **Vitamin C:** The fruit of *Lycium barbarum* L. contains 0.5% of a novel stable precursor of ascorbic acid, which may theoretically increase serum ascorbic acid levels (Toyada-Ono et al., 2005; Toyada-Ono et al., 2004).
- **Weight loss agents:** In a clinical trial of GoChi™ fruit juice, the juice resulted in an increased reduction in waist circumference, but not a reduction in body weight, in subjects that were also exercising (Amagase & Nance, 2011). In human research, GoChi™ lacked a statistically significant effect on body weight, BMI, and body fat (Amagase & Nance, 2008).
- **Zeaxanthin:** In healthy volunteers, goji increased plasma zeaxanthin levels (Breithaupt et al., 2004; Bucheli et al., 2011; Cheng, Chung, Szeto, & Benzie, 2005; Sin, Liu, & Lam, 2013).
- **Zinc:** In animal research, *Lycium barbarum* polysaccharides (LBP-4) increased the level of zinc in muscle and bone (Zhang et al., 2002).

Goji/Food Interactions

- **Iron-containing foods:** When fed to weanling mice, *Lycium barbarum* polysaccharides(LBP-4) enhanced the content of zinc and iron in pygal muscles and femora and reduced their body weight (Zhang et al., 2002).
- **Vitamin C-containing foods:** The fruit of *Lycium barbarum* L. contains 0.5% of a novel stable precursor of ascorbic acid, which could theoretically increase serum ascorbic acid levels (Toyada-Ono et al., 2005; Toyada-Ono et al., 2004).
- **Zinc-containing foods:** In animal research, *Lycium barbarum* polysaccharides (LBP-4) increased the level of zinc in muscle and bone (Zhang et al., 2002).

Goji/Lab Interactions

- **Antibodies (serum):** In animal research, *Lycium* increased serum IgA and IgG levels (Lin et al., 2006). In human research, results from available randomized controlled trials suggest that wolfberry alters immune response, such as increasing the number of lymphocytes and levels of interleukin-2 and immunoglobulin G (Amagase et al., 2009; Vidal et al., 2012).
- **Blood pressure:** In animal research, *Lycium* constituents had antihypertensive effects (Jia et al., 1998). However, in human research, GoChi™ lacked a statistically significant effect on systolic and diastolic blood pressure (Amagase & Nance, 2008).
- **Cytokines:** In human research, results from available randomized controlled trials suggest that wolfberry alters immune response, such as increasing the number of lymphocytes and levels of interleukin-2 and immunoglobulin G (Amagase et al., 2009). In animal research, wolfberry decreased IL-5 and GRO/KC (IL-8 rat homologue) (Stoner et al., 2010).
- **INR:** In case reports of individuals stabilized on warfarin, *Lycium barbarum* L. fruit elevated the international normalized ratio (INR) (Lam et al., 2001; Leung et al., 2008; Rivera, Ferro, Bursua, & Gerber, 2012).
- **Insulin:** In animal research, *Lycium barbarum* increased insulin sensitivity (Zhao et al., 2005).
- **Lipid panel:** In animal research, *Lycium barbarum* decreased plasma cholesterol and plasma triglycerides (Luo et al., 2004; Zhao et al., 2005).

- **Liver panel:** In animal research, *Lycium chinense* Miller (Solanaceae) had hepatoprotective effects and decreased levels of serum aspartate and alanine aminotransferase (AST and ALT) and alkaline phosphatase (ALP) (Ha et al., 2005).
- **Platelet counts:** In chemotherapy-induced myelosuppressive and irradiated mice, *Lycium barbarum* polysaccharide enhanced peripheral platelet counts (Gong et al., 2005; Hsu et al., 1999).
- **Red blood cell counts:** In chemotherapy-induced myelosuppressive and irradiated mice, *Lycium barbarum* polysaccharide enhanced peripheral red blood cell counts (Gong et al., 2005; Hsu et al., 1999).
- **Serum ascorbic acid levels:** The fruit of *Lycium barbarum* L. contains 0.5% of a novel stable precursor of ascorbic acid, which with theoretically increase serum ascorbic acid levels (Toyada-Ono et al., 2005; Toyada-Ono et al., 2004).
- **Serum glucose levels:** In animal study, *Lycium barbarum* decreased plasma glucose and 30-min postprandial glucose levels (Luo et al., 2004; Shabana et al., 1990; Wu et al., 2006; Zhao et al., 2005).
- **Serum hormone levels:** In vitro, *Lycium barbarum* regulated and increased secretion of male sexual hormones (Luo et al., 2006).
- **Serum levels of cytochrome P450-metabolized agents:** In vitro, a tea of *L. barbarum* L. weakly inhibited S-warfarin metabolism by CYP2C9 (Lam et al., 2001).
- **T cell counts:** In animal research, *Lycium barbarum* polysaccharide significantly increased the numbers of CD4(+) and CD8(+) T cells (He et al., 2005). In human research, results from available randomized controlled trials suggest that wolfberry alters immune response, such as increasing the number of lymphocytes and levels of interleukin-2 and immunoglobulin G (Amagase et al., 2009).
- **White blood cell counts:** In irradiated mice, intraperitoneal *Lycium chinense* root increased leukocyte counts (Hsu et al., 1999).
- **Zeaxanthin levels:** In healthy volunteers, goji increased plasma zeaxanthin levels (Breithaupt et al., 2004; Bucheli et al., 2011; Cheng et al., 2005; Sin et al., 2013).

Goji/Nutrient Depletion

- **Glucose:** In animal research, *Lycium barbarum* decreased plasma glucose and 30-min postprandial glucose levels (Luo et al., 2004; Shabana et al., 1990; Wu et al., 2006; Zhao et al., 2005).
- **Lipids:** In animal research, *Lycium barbarum* decreased plasma cholesterol and plasma triglycerides (Luo et al., 2004; Zhao et al., 2005).

MECHANISM OF ACTION

Pharmacology

- **Constituents:** More than 100 constituents have been identified in the berries, leaves, root bark, and roots of wolfberry. The most abundant and well-researched constituents to date are the carotenoids, the antioxidants, and the polysaccharides. Dried goji berries, aqueous extracts, and many constituents of goji berries, including glycoconjugates, polysaccharide, and total flavonoids, have demonstrated antioxidant properties (Huang et al., 1999, 2001; Ni et al., 2004; Peng

et al., 2001; Ren et al., 1995; Wu et al., 2004). Goji berries also contain a significant quantity of a precursor to vitamin C. Other goji constituents of particular interest include (1) monomenthyl succinate, a molecule that provides the cooling effect of menthol without the burning sensation (Hiserodt et al., 2004), (2) scopoletin, a component from the fruit of *Lycium barbarum* that demonstrated the greatest inhibition activity (IC_{50}) on PC3 cell proliferation in vitro (Liu et al., 2000), and (3) three pyrrole derivatives (two of which demonstrated hepatoprotective effects comparable to silybin) (Chin et al., 2003).

- **Carotenoids:** Goji berries contain both lutein and zeaxanthin (zeaxanthin dipalmitate, 3R,3R'-zeaxanthin palmitate, zeaxanthin ester), and they are reputed to be one of the richest natural sources of zeaxanthin (Benzie et al., 2006; Breithaupt et al., 2004; Gribovski-Sassu et al., 1969; Kim et al., 1997b; Peng et al., 2005; Weller & Breithaupt, 2003). The range of carotenoid concentration in various fructus *Lycii* has been estimated to be 0.03%–0.5%. Zeaxanthin palmitate is the predominant carotenoid in fructus *Lycii* and forms 31%–56% of its carotenoid content (Peng et al., 2005). Both lutein and zeaxanthin are oxygenated carotenoids that have antioxidant and blue light-absorbing properties. These compounds accumulate in the macula, where they may help to prevent age-related macular degeneration (Breithaupt et al., 2004; Cheng et al., 2005).
- **Polysaccharides:** According to some experts, polysaccharides are “the most important functional constituent in *Lycium barbarum* fruits” (Luo et al., 2006). *Lycium barbarum* polysaccharides have been shown to have a wide variety of physiological effects, primarily in animal studies. These properties include the following: anti-infertility, antioxidant, anticancer, antihypertensive, antilipidemic, antimyelosuppression, immune support, radiation protection, and regulation of blood glucose and insulin sensitivity (Du et al., 2004; Gan et al., 2003; Gong et al., 2005; He et al., 2005; Huang et al., 2003; Jia et al., 1998; Lu & Cheng, 1991; Luo et al., 1999; 2004, 2006; Wu et al., 2006; Zhang et al., 2005; Zhao, Alexeev, Chang, Greenburg, & Bojanowski, 2005).
- **Vitamin C:** A stable precursor of ascorbic acid (vitamin C), called 2-O-(beta-D-glucopyranosyl) ascorbic acid, has been isolated from both the ripe fresh fruit and dried fruit of *Lycium barbarum* L. The content of ascorbic acid in the dried fruit is 0.5%, which is equivalent to the vitamin C content of fresh lemons (Toyoda-Ono et al., 2005; Toyoda-Ono et al., 2004).
- **Fruits:** Constituents that have been identified in the fruits include 2-O-(beta-D-glucopyranosyl) ascorbic acid, arabinogalactan proteins, atropine, betaine, beta-sitosterol, carotenoids, cerebroside (LCC), daucosterol, glucose, glycoconjugates, glycolipids, glycoprotein, isoscapoletin, lutein, p-coumaric acid, polysaccharides, three pyrrole derivatives, scopoletin, zeaxanthin dipalmitate, 3R,3R'-zeaxanthin palmitate, and zeaxanthin ester (Adams et al., 2006; Breithaupt et al., 2004; Chin et al., 2003; Gribovski-Sassu et al., 1969; Huang et al., 1998; Huang et al., 1999; Jung, Chin, Kim, & Kim, 2005; Kim, Lee, Kim, Lee, & Kim, 2000; Peng et al., 2005; Qin, Yamauchi, Aizawa, Inakuma, & Kato, 2001; Shin, Cho, Kim, Park, & Park, 1999; Toyoda-Ono et al., 2004; Weller & Breithaupt, 2003; Xie et al., 2001).

- Kim et al. have identified (1-O-(beta-D-glucopyranosyl)-(2S,3R,4E,8Z)-2-N-palmitoyl tadecaspinga-4,8-diene; LCC) from the fruits of *Lycium chinense* Mill. (Kim et al., 1999).
- Kim et al. have isolated 1-O-beta-D-glucopyranosyl-(2S, 3R,4E,8Z)-2-N-palmitoyloctadecaspinga-4,8-dienine+ ++ and 1-O-beta-D-glucopyranosyl-(2S,3R,4E,8Z)-2-N-(2'-hydroxypalmitoyl) octadecaspinga-4,8-dienine from the fruits of *Lycium chinense* (Kim et al., 1997a).
- **Leaves:** Constituents that have been identified in the leaves include beta D-glucoside, beta-sitosterol, and vitamin E (Ching & Mohamed, 2001; Imai, Murata, Fujioka, & Goto, 1963).
- **Root bark:** Four phenolic amides have been identified in the root bark of *Lycium chinense* Miller (Han et al., 2002; Lee et al., 2004).
- **Roots:** Constituents that have been identified in the roots include beta-sitosterol, 14 calystegines, cycloheptane, E-ferulic acid octacosylester, polyhydroxylated piperidine alkaloids, polyhydroxytropans, and scopoletin (Asano et al., 1997; Zhou, Xu, & Wang, 1996). (+)-Lyoniresinol-3alpha-O-beta-D-glucopyranoside has also been isolated from the root bark of *Lycium chinense* Miller (Lee et al., 2005).
- **Unspecified plant part:** Alpha-(1->6)-D-glucans, a-(1->4)-D-polygalacturonans, acyclic diterpene glycosides, betaine, bis (dihydrocaffeoyl) spermine isomers, coumarin, cyclic peptides, ferredoxins, flavonoids, glycoconjugate, glycoprotein, three glycosides, hesperidin, kaempferol, lyciumins A-D, lyciumosides I-III, polysaccharide, taurine, vanillic acid, vitamin E, and withanolides have also been identified in goji (Ching & Mohamed, 2001; Deng et al., 2003; Du et al., 2004; Duan et al., 2001; Gan & Zhang, 2001; Hansel & Huang, 1977; Hansel, Huang, & Rosenberg, 1975; Huang et al., 1999; Lee et al., 2004; Mino, 2002; Parr, Mellon, Colquhoun, & Davies, 2005; Peng & Tian, 2001; Peng et al., 2001; Shin et al., 1999; Wei, Zhang, Zhang, & Liu, 2001; Xie & Zhang, 1997; Yahara et al., 1993; Zhi, Zheng, Chen, & He, 2004).
- **Alzheimer's disease effects:** Researchers studied the effect of the traditional Chinese herbs Dangguishaoyaosan and Chaihujialonggumulitang, and two "herbs" (CHP I and CHP II) developed by the authors, in a mouse model of Alzheimer's disease (Sun, Hu, Zhang, Li, & He, 2003). Behavioral and histochemical tests, with piracetam serving as control, demonstrated that CHP II "has profound curative effects on improving the memory and cognitive function in an animal model of Alzheimer's disease-like disease."
- **Antiaging effects:** In a D-galactose mouse aging model, treatment with *Lycium barbarum* polysaccharide (LBP) resulted in decreased levels of serum AGE, decreased hydroxyproline concentration in mouse skin, and decreased spontaneous motor activity (Deng et al., 2003). At the same time, this treatment enhanced learning and memory abilities, the SOD activity of erythrocytes, lymphocyte proliferation, and IL-2 activity. The authors concluded that LBP may inhibit nonenzyme glycation in a D-galactose-induced mouse aging model in vivo.
- The effect of a water extract of goji fruit (WB) on DNA synthesis of the aging-youth 2BS fusion cells was investigated (Wu et al., 2003). In the media containing 0.025 (v/v) WB water extract, 2BS cells could be cultured continuously for $61.0 \pm$

2.9 passages versus 49.0 ± 2.6 passages in controls. In addition, when aging 2BS cells were treated with WB for 2 hr, denucleated and fused with young 2BS cells, there was a significantly higher incorporation of $[^3\text{H}]\text{TdR}$ than in untreated control cells ($p < .01$). The authors concluded that WB may prolong the life span of 2BS cells and accelerate the rate of DNA synthesis in aging-youth 2BS fusion cells.

- **Antiasthma effects:** In a clinical trial with 35 convalescing asthma patients, administration of a Chinese herbal decoction (Invigorating Kidney) resulted in improvement in various parameters of maximal expiratory flow-volume curve. These results indicate that this herbal formula helps to reverse airway obstruction in asthmatics in the convalescent stage (Fu, 1989). These 35 patients were chosen from a larger group of 66 asthmatics after measurement of maximal expiratory flow-volume curve (MEFV) revealed abnormal results for FEV, PEF, V75, V50, and V25 compared to healthy persons. These results indicated the presence of airway obstruction (primarily small airways) in these individuals. Invigorating Kidney formula was administered in the following daily dosage for 10 weeks: *Viscum coloratum* 15 g, *Psoralea corylifolia* 15 g, *Eucommia ulmoides* 15 g, *Lycium chinense* 9 g, *Tussilago farfara* 15 g, *Artemisia capillaris* 9 g, and *Pogostemon cablin*. Results showed that various parameters of MEFV “improved to some extent,” indicating that it is possible to reverse airway obstruction in convalescing asthmatics with this Chinese herbal formula.
- **Anticancer effects:** In a before-and-after comparison trial with 79 advanced cancer patients, *Lycium barbarum* polysaccharides (LBP) versus LBP combined with LAK/IL-2 (lymphokine-activated killer cells) versus LAK/IL-2 alone resulted in a response rate of 40.9% versus 16.1% in the group treated with LAK/IL-2 alone ($p < .05$) (Cao et al., 1994). The combination treatment resulted in a greater increase in NK and LAK cell activity, as well as a significantly longer “mean remission.” Researchers observed objective regression of cancer in patients with malignant melanoma, renal cell carcinoma, colorectal carcinoma, lung cancer, nasopharyngeal carcinoma, and malignant hydrothorax. They concluded that LBP “may be used as an adjuvant in the biotherapy of cancer.”
- In animal research, wolfberry inhibited N-nitrosomethylbenzylamine (NMBA)-induced tumorigenesis in the rat esophagus (Stoner et al., 2010). Mechanisms of action may involve a decrease in IL-5 and GRO/KC (IL-8 rat homologue) and an increase in serum antioxidant capacity.
- In vitro research has demonstrated that a hot water extract of *Lycium barbarum* (LBE) dose-dependently inhibited proliferation of rat hepatocellular carcinoma cells (HCC), as well as human (HCC). LBE also stimulated p53-mediated apoptosis in rat HCC cells (Chao et al., 2006). *Lycium barbarum* polysaccharide (LBP), extracted from *Lycium barbarum*, has been shown to inhibit QGY7703 cell growth via S phase cycle arrest and apoptosis induction (Zhang et al., 2005). This study suggests that the antiproliferative activity of LBP in QGY7703 cells may occur via induction of cell cycle arrest and increased intracellular calcium in the apoptotic system.
- In vitro, LBP arrested inhibited growth of cancer cells with cell cycle arrest at the G0/G1 or S phases (Miao et al., 2010).

- **Antidiabetic effects:** Four weeks of treatment with polysaccharides extracted from *Lycium barbarum* (LBP) led to decreased levels of blood glucose, malondialdehyde (MDA) and nitric oxide (NO), and increased superoxide dismutase (SOD) in serum of fasting type 2 diabetic rats with DNA damage (Wu et al., 2006). LBP also reduced cellular DNA damage in peripheral lymphocytes of NIDDM rats, possibly by reducing the level of oxidative stress. Researchers investigated the effect of three weeks of treatment with *Lycium barbarum* polysaccharide (LBP) on lipid profiles and insulin resistance in streptozotocin-induced type 2 diabetic rats (Zhao et al., 2005). LBP treatment resulted in a significant decrease in plasma cholesterol, plasma triglycerides, fasting plasma insulin, and 30-min postprandial glucose levels. LBP also significantly increased the Insulin Sensitivity Index in these animals. Researchers identified increased cell-surface level of GLUT4 (glucose transporter 4) and improvements in GLUT4 trafficking and intracellular insulin signaling as possible mechanisms of action. In type 2 diabetic rats receiving LBP treatment, GLUT4 content in the plasma membrane was significantly higher than in control type 2 diabetic rats ($p < .01$).
- *Lycium barbarum* fruit water decoction, crude polysaccharide extracts (crude LBP), and purified polysaccharide fractions (LBP-X) were investigated in alloxan-induced diabetic or hyperlipidemic rabbits for their hypoglycemic and hypolipidemic effects (Luo et al., 2004). Data were obtained by measuring blood glucose and serum lipid parameters in sequential trials. In addition, total antioxidant capacity was assessed using Trolox equivalent antioxidant capacity (TEAC) and an oxygen radical absorbance capacity (ORAC) assay. Results after 10 days of treatment showed that the three *Lycium barbarum* fruit extracts or fractions significantly reduced blood glucose levels, as well as serum total cholesterol (TC) and triglyceride (TG) concentrations, while simultaneously markedly increasing high-density lipoprotein cholesterol (HDL-C) levels. LBP-X showed a more significant hypoglycemic effect than that of the water decoction and crude LBP, but its hypolipidemic effect seemed to be weaker. All three *Lycium barbarum* extracts or fractions possessed antioxidant activity. However, the water and methanolic fruit extracts and crude polysaccharide extracts exhibited stronger antioxidant activity than purified polysaccharide fractions. These crude extracts were identified as being rich in antioxidants (e.g., carotenoids, riboflavin, ascorbic acid, thiamine, nicotinic acid). The authors stated that several monosaccharides and 17 amino acids are the major bioactive constituents producing the hypoglycemic effect of *Lycium barbarum* polysaccharides (glycoconjugates). Possible active principles for the hypolipidemic effect are both polysaccharides and vitamin antioxidants from *Lycium barbarum* fruits.
- Thirty-one plants from 17 families were collected from different parts of Egypt (Shabana et al., 1990). Extracts from 21 of these plants were administered orally to normal rats, and 15 extracts were tested on fasting and on alloxanized rats. The results were compared to a positive control, a standard oral hypoglycemic drug (Daonil, Hoechst). Eight plants (*Lycium shawii*, *Salvia* (*S.*) *aegyptiaca*, *Pergularia tomentosa*, *Convolvulus* (*C.*) *althaeoides*, *Haloxylon salicornicum*, *Ephedra alata*, *Scrophularia deserti*, and *Crotalaria aegyptiaca*) exhibited persistent hypoglycemic effects in normal animals. Only four out of the 15 plant extracts tested

on alloxanized diabetic rats showed hypoglycemic effects more potent than those of the administered dose of Daonil: *Matthiola livida*, *S. aegyptiaca*, *Astragalus* species, and *Arthrocnemum glaucum*.

- **Antifatigue effects:** LBP-X, a purified component of *Lycium barbarum* polysaccharide, was tested on mice in five different doses ranging from 5–100 mg/kg daily. This constituent induced resistance to fatigue and elimination of fatigue, as well as adaptability to exercise load (Luo et al., 2000). Physiological markers included increased storage of muscle and liver glycogen, increased LDH activity before and after swimming, modulation of the increase in blood urea nitrogen (BUN) after strenuous exercise, and an accelerated clearance of BUN after exercise.
- **Antifungal effects:** Dihydro-N-caffeoyltyramine (1), *trans*-N-feruloyloctopamine (2), *trans*-N-caffeoyltyramine (3), and *cis*-N-caffeoyltyramine (4) are four phenolic amides isolated from an ethyl acetate extract of the root bark of *Lycium chinense* Miller (Lee et al., 2004). All four constituents had antifungal effects and impeded the dimorphic transition of *Candida albicans*. Compounds 1–3 were potent at 5–10 mcg/ml and demonstrated no hemolytic activity against human erythrocyte cells. Compound 4 was active at 40 mcg/ml.
- **Antiglaucoma effects:** Using an ocular hypertension (OH) model in rats, oral administration of *Lycium barbarum* (250–280 g) significantly reduced the loss of retinal ganglion cells (RGCs), although elevated intraocular pressure (IOP) was not significantly altered (Chan et al., 2007). Rats fed with the 1 mg/kg extract showed almost no pressure-induced loss of RGCs. This is the first in vivo report showing the neuroprotective properties of *Lycium barbarum* L. extract in a rat model of glaucoma.
- **Antihypertensive effects:** In the present study, researchers investigated the effects of *Lycium barbarum* polysaccharide (LBP) on endothelial function in the two-kidney, one-clip model of hypertension in rats (Jia et al., 1998). The results showed that treatment with 10% LBP resulted in a significant prevention of the increase in blood pressure in hypertensive rats (HR). The contraction of phenylephrine (PE) in isolated aortic rings of LBP-treated rats was reduced compared with HR. This difference of PE-induced vasoconstriction among groups was abolished when the endothelium was removed. When aortic rings from LBP-treated rats were incubated in vitro with methyl blue (MB) or N-nitro-L-arginine methyl ester (L-NAME), the magnitude of PE-induced contraction increased. In LBP-treated rats, the response to acetylcholine (ACh) significantly increased, but there was no significant difference in the response to nitroprusside between groups. In RH, pretreatment with L-arginine partially restored ACh-induced relaxation but had no effect in LBP-treated rats. The authors proposed that the role of LBP in decreasing vasoconstriction to PE may be mediated by increased effects from and/or the production of endothelium-derived relaxation factor (EDRF), which in turn, may be related to an increase in the substrate of EDRF.
- In human research, GoChi™ lacked a statistically significant effect on systolic and diastolic blood pressure (Amagase & Nance, 2008).
- **Anti-inflammatory effects:** A traditional Chinese medicine (TCM) compound consisting of an extractive and three herbal products (herba *Epimedii*, fructus

Cnidii, and fructus *Lycii*) was studied for its anti-inflammatory effect in three animal models (Wei et al., 2002). Carrageenan-induced paw edema, cotton-ball granuloma, and adjuvant induced arthritis in rats were chosen to study the anti-inflammatory effect of the TCM agent. Results showed that the TCM compound had a marked inhibitory effect on edema induced by all three types of inflammation in rats. The inhibitory rate of the TCM compound at doses of 0.20, 0.40, and 0.80 g/kg in the granuloma model was over 25% at 1 hr after oral administration. At 6 hr, the inhibitory rates were 23.8%, 22.7%, and 39.7%. In addition, the TCM compound also demonstrated both a significant preventive, as well as therapeutic, effect on adjuvant induced arthritis in rats. Researchers observed improvements in the pathological changes of the animal joints with the induced arthritis.

- **Antileukemia effects:** *Lycium barbarum* polysaccharide (LBP-X) has been shown to inhibit the growth of human leukemia HL-60 cells in vitro (Gan et al., 2001). LBP-X (20, 100, 500, 1,000 mg/L) inhibited the growth of HL-60 cells in a dose-dependent manner and decreased the membrane fluidity of the cell. Researchers proposed that the apoptosis of HL-60 cells induced by LBP-X may be its mechanism of action for antitumorogenesis.
- **Antimicrobial effects:** (+)-Lyoniresinol-3 α -O-beta-D-glucopyranoside, isolated from an ethyl acetate extract of the root bark from *Lycium chinense* Miller, demonstrated strong antimicrobial activity against antibiotic-resistant bacterial strains, methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from patients, and the human pathogenic fungus *C. albicans* (Lee et al., 2005). (+)-Lyoniresinol-3 α -O-beta-D-glucopyranoside showed no hemolytic effect on human erythrocytes.
- **Antiosteoporosis effects:** Researchers screened 60 MeOH and water extracts of natural crude drug for their ability to stimulate osteoblast proliferation. Four MeOH extracts (*Cynomorium songaricum*, *Drynaria fortunei*, *Lycium chinense*, *Rehmannia glutinosa*) and seven water extracts (*Cornus officinalis*, *Dendrobium nobile*, *Dioscorea spongiosa*, *Drynaria fortunei*, *Eucommia ulmoides*, *Lycium chinensis*, and *Viscum coloratum*) showed potent activities that were then evaluated for the inhibition of osteoclast formation (Yin et al., 2004).
- **Antioxidant effects:** In human research, goji increased levels of superoxide dismutase (SOD) and glutathione peroxidase, and decreased levels of malondialdehyde (MDA) (Amagase et al., 2009). In human research, Lacto-Wolfberry (a proprietary milk-based formulation of goji) increased plasma zeaxanthin levels and the antioxidant capacity (Bucheli et al., 2011).
- In animal research, wolfberry resulted in an increase in serum antioxidant activity (Stoner et al., 2010).
- Glycoconjugates and their glycans from *Lycium barbarum* L. were tested for their effect on inhibiting low-density lipoprotein (LDL) peroxidation in a Cu(2+)-induced oxidation model that assessed the oxidative production of thiobarbituric acid reactive substances (TBARS) and the LDL electrophoresis migration on agarose gel (Huang et al., 2001). Results showed that the glycoconjugates may inhibit LDL peroxidation (glycoconjugate LbGp5 showed the best effect), while their glycans showed no effects.

- LbGp2 has demonstrated antioxidant effects and effectively scavenged the superoxide anion produced by the DMSO-NaOH system (Peng et al., 2001). LbGp2 was shown to have good immunoactivity and antioxidative activity.
- In this work, the changes in electrical parameters of the cell membrane of *Xenopus* oocytes were incubated in a frog Ringer solution containing a free radical-producing system for 6 hr (Zhang, 1993). Results showed that the resting membrane potential was raised and that the membrane resistance and time constant decreased. These effects demonstrate that the effects of free radicals on cells may be prevented and reversed by incubation with superoxide dismutase or *Lycium barbarum* polysaccharide.
- In a rat model of H₂O₂-induced lipid peroxidation, the following ingredients inhibited the lipid peroxidation of RBC membrane in descending order: fructus *Lycii*/LbL.dry(FL/LbL.dry) > polysaccharide FL/LbL > residue FL/LbL > betaine (Ren et al., 1995).
- Aqueous extracts of three popular ingredients of traditional Chinese medicine, namely *Angelica sinensis* (AS), *Lycium barbarum* (LB), and *Poria cocos* (PC), were evaluated for their antioxidant properties (Wu et al., 2004). All extracts displayed antioxidant activities in a concentration-dependent manner. The inhibitory effect on FeCl₂-ascorbic acid-induced lipid peroxidation in rat liver homogenate in vitro was LB > AS > PC. The range of superoxide anion scavenging activity was 28.8%–82.2%, and antiperoxidative activity ranged from 38.0% to 84.5%. LB extract exhibited the lowest IC₅₀ values (0.77–2.55 mg/ml) in all model systems tested in this study. The present study indicates that LB extract is the strongest inhibitor of malondialdehyde formation in rat liver homogenate and had the greatest superoxide anion-scavenging and antiperoxidative activity of the three extracts tested.
- Researchers studied the effects of *Lycium barbarum* polysaccharides (LBP) on xanthine oxidase hypoxanthine-induced (XO-HPX) free radical damage in *Xenopus laevis* oocyte membranes (Zhang et al., 1997). After more than 4 hr of exposure to the (XO-HPX) reaction system, the acetylcholine receptor (Ach) polarization decreased, the rise time prolonged, the degree of depolarization decreased, and the decay half-time shortened. *Lycium barbarum* polysaccharide (LBP) was found to improve the passive electrical membrane parameters of the injured membrane, but it did not lead to the recovery of Ach depolarization. The authors suggested that LBP may antagonize the action of free radicals on the membrane, although it is not effective in reversing muscarine receptor injury.
- *Lycium barbarum* fruit water decoction, crude polysaccharide extracts (crude LBP), and purified polysaccharide fractions (LBP-X) were investigated in alloxan-induced diabetic or hyperlipidemic rabbits for their hypoglycemic and hypolipidemic effects (Luo et al., 2004). In addition, total antioxidant capacity was assessed using Trolox equivalent antioxidant capacity (TEAC) and an oxygen radical absorbance capacity (ORAC) assay. Results after 10 days of treatment showed that all three *Lycium barbarum* extracts or fractions possessed antioxidant activity. However, the water and methanolic fruit extracts and crude polysaccharide extracts exhibited stronger antioxidant activity than purified polysaccharide fractions.

- The efficacy of *Lycium barbarum* polysaccharides (LBP) in scavenging hydroxyl free radicals was investigated (Ni et al., 2004). The scavenging rates of LBP to hydroxyl free radical were 18.64% at 0.25 mg/ml and 87.29% at 1.0 mg/ml. It is unclear whether the lower concentration or the higher concentration was effective.
- The ESR-spin trapping technique and the inhibitory effects on heat output of both polymorphonuclear leukocyte (PMN) respiration burst and L1210 cells were used to study the scavenging effects of total flavonoids of *Lycium barbarum* L. (TFL) (Huang et al., 1998). The scavenging rate of O₂⁻ by TFL in the xanthine/xanthine oxidase (Xan/XO) system was 0%–51%. The scavenging rate of OH (produced in Fenton reaction) by TFL was between 20% and 72%. In both cases these effects were concentration dependent. In addition, TFL completely inhibited the heat output from PMA-stimulated PMN and inhibited the heat output from L1210 cells.
- The effect of *Lycium barbarum* L. (LB) on free radical injury caused by hypoxia was tested in mice (Li et al., 2002). Fifty-six mice were fed with LB or distilled water by tube feeding for 16 days. Results indicated that LB could not increase hypoxic tolerance or prolong survival, but it did increase the activities of superoxide dismutase (SOD), catalase (CAT), and total antioxidative capacity when compared to the control group ($p < .05$). The pigment of *Lycium ruthenicum* was evaluated for its antioxidant activity (Li et al., 2006). Results showed that the pigment of *L. ruthenicum* effectively scavenged DPPH and effectively inhibited H₂O₂-induced hemolysis of mouse erythrocytes. The tested substance enhanced serum resistance to reactive oxygen species. In addition, the concentration of MDA (lipid peroxidation product) in mouse liver and the swelling of mouse liver mitochondria were reduced. These outcomes indicate that *L. ruthenicum* pigment has antioxidant effects at the tested concentration.
- Researchers investigated the effect of zeaxanthin dipalmitate (ZD), a carotenoid from *Lycium chinense* fruit on bile duct ligation scission (BDL)-induced hepatic fibrosis in rats (Kim et al., 2002). Results showed that treatment of BDL rats with ZD at a dose of 25 mg/kg of body weight significantly reduced the following parameters: the activities of aspartate transaminase ($p < .05$) and alkaline phosphatase ($p < .001$) in serum, collagen deposition ($p < .01$), levels of thiobarbituric acid-reactive substances, and 4-hydroxyproline levels. Therefore, ZD effectively inhibited hepatic fibrosis in BDL rats, at least in part via its antioxidative activity.
- The protective effect of *Lycium barbarum* polysaccharides (LBP) on hydrogen peroxide-induced DNA oxidative damage to testicle cells was investigated (Huang et al., 2003). Testicle cells were first treated by different concentrations of LBP for 1 hr and then cultured with 100 μ mol/L of H₂O₂ for 25 min. Researchers used single-cell gel electrophoresis to detect DNA strand breakage and assess the protective effects of LBP against oxidative damage in cultured cells. Results showed that pretreatment with LBP (50, 100, 200, 400 μ g/ml) significantly decreased the frequency of cells with DNA damage from oxidative stress. Total flavonoids from *Lycium barbarum* L. (TFL) were tested for their protective effects on lipid peroxidation in mitochondria and red blood cells (RBC) induced by oxygen radicals produced by the Fe²⁺ cysteine system (Huang et al., 1999).

TFL significantly inhibited mitochondrial lipid peroxidation (measured as malondialdehyde, MDA) with a dose-response relation between the concentrations of 0.025 and 2.0 mg/ml. TFL also effectively protected the fluidity of the mitochondrial membrane. Observation with a scanning electron microscope showed that damage to the shape of RBC in the Fe²⁺ system was prevented with the addition of TFL.

- **Antiproliferative effects:** The active components from the fruit of *Lycium barbarum* were extracted and tested for their inhibition activity (IC₅₀) on PC3 cell proliferation in vitro (Liu et al., 2000). Results showed that scopoletin is the most active component isolated from the fruit of *L. barbarum* for inhibiting PC3 cell proliferation.
- **Antitumor effects:** The immunomodulatory effect of a polysaccharide-protein complex from *Lycium barbarum* (LBP3p) on the immune system was investigated in S180-bearing mice (Gan et al., 2004). After inoculation with S180 cell suspension, mice were treated orally with LBP3p (5, 10, and 20 mg/kg) for 10 days. Results showed that LBP3p significantly inhibited the growth of transplantable sarcoma S180 and increased the following parameters: macrophage phagocytosis, the form of antibody secreted by spleen cells, spleen lymphocyte proliferation, CTL activity, and IL-2 mRNA expression level. In addition, lipid peroxidation in S180-bearing mice was reduced. These effects were not dose-dependent in a linear fashion. The 10 mg/kg dose was the most effective of the three doses studies. The effects of *Lycium barbarum* polysaccharide (LBP) on tumor microenvironment, T-lymphocyte subsets and dendritic cells, and the mechanisms for intervention of tumor immune escape by LBP were studied in H22-bearing mice (He et al., 2005). After two weeks of oral ingestion of LBP, there was a significant increase in the numbers of CD4(+) and CD8(+) T cells in tumor-infiltrating lymphocytes (TIL) when compared to those in the model control group ($p < .05$). In the control group, the number of dendritic cells in tumor microenvironment decreased markedly. The LBP-treated group showed an increased number of dendritic cells and B7-1 expression, but the differences between these two groups were not significant. The authors proposed that LBP has antitumor effect by increasing the numbers of CD4(+) and CD8(+) T cells in TIL to relieve immunosuppression and enhance the antitumor function of the immune system.
- **Antiviral effects:** Researchers screened 60 kinds of commonly used Chinese medicines for their ability to depress the release of Lambda phage from lyso-genic strains in the induct test (Wang et al., 1991). Eleven Chinese medicines, including *Codonopsis radix*, *Polygonatum radix*, and fructus *Lycium*, showed the strongest inhibitory effects. They also showed an inhibitory dose-effect response on SOS response in the SOS chromotest. They also decreased the frequency of gene conversion in *S. cerevisiae* in the presence of hydroxyurea.
- **Apoptosis activity:** *Lycium barbarum* (LB) has been shown to dose-dependently inhibit the hydrocortisone (HYD)-induced apoptosis of rat spleen cells (Lu, Xian, Lu, Wu, & Gu, 1999).
- **Cardioprotective effects:** The protective effect of *Lycium barbarum* glycopeptide (LbGp) on calcium overload was investigated in the hypoxia KCl injury

model in cultured neonatal rat cardiomyocytes (CMs) (Xu et al., 2005). Three groups of cells (a normal control, a hypoxia group, and a Blip-treated group) (CMs) were cultured in an incubator ventilated with 95% N₂ and 5% CO₂ with or without LbGP. Outcome measures were the viability of CMs under hypoxia and the intracellular free calcium concentration in cardiomyocytes. Results indicated that LbGp is able to increase the survival ratio and inhibit hypoxia and high potassium-induced enhancement of the intracellular free calcium concentration in cardiomyocytes. One of the mechanisms of action is via the effects of LbGp on L-type calcium channels.

- **Cytoprotective effects:** The intention of this study was to clarify whether the extract from *L. barbarum* (LBG) is a simple antioxidant exhibiting cytoprotective effects, or whether LBG extract protects neurons via mechanisms independent of antioxidative effects (Yu et al., 2006). By using a reducing agent, dithiothreitol (DTT), researchers found that LBG exhibits cytoprotective effects against reducing stress by lowering the DTT-induced LDH release and caspase-3 activity. Investigators also showed that LBG attenuates DTT-induced PERK phosphorylation in endoplasmic reticulum (ER). Therefore, *L. barbarum* extract is not simply an antioxidant; it may also exhibit cytoprotective effects against reducing stress by DTT.
- *Lycium barbarum* (LB) has been shown to dose-dependently inhibit the hydrocortisone (HYD) induced apoptosis of rat spleen cells (Lu et al., 1999).
- **Dermatologic effects:** In vitro, a combination of Himalayan actives including goji berries attenuated ultraviolet B (UVB)-induced cell apoptosis of skin organ epidermis and decreased TNF-alpha secretion (Wineman et al., 2012).
- **Exercise effects:** In human research, *L. barbarum* increased VO₂ (Amagase & Nance, 2011).
- **Fertility effects:** A component of *Lycium chinense* Miller has been found to induce ovulation in adult female rabbits (Suzuki et al., 1972).
- Fructus *Lycii*, the fruits of *Lycium barbarum* L. (Solanaceae), are used by Chinese physicians for treatment of infertility (Wang et al., 2002). This in vitro research study has demonstrated that fructus *Lycii* polysaccharides (FLPS) inhibit hyperthermia- and time-induced structural damage in mouse seminiferous epithelium. Furthermore, FLPS delayed apoptosis in this system, both at normothermic and hyperthermic culture conditions. FLPS was found to be a potent inhibitor of both ultraviolet light-induced lipid peroxidation and cytochrome c reduction by free radicals. Since it has been reported that oxidative stress is a major cause of structural damage and apoptosis in hyperthermic testes, the authors proposed that the protective effect of FLPS on time- and hyperthermia-induced testicular degeneration in vitro is due to its antioxidant properties.
- **Hematologic effects:** This study investigated the effects of *Lycium barbarum* polysaccharide (LBP) on irradiation- or chemotherapy-induced myelosuppressive mice in vivo and cultured peripheral blood mononuclear cells (PBMCs) in vitro (Gong et al., 2005). For the in vivo experiment, researchers irradiated mice with a sublethal dose of 550cGy X-rays or intraperitoneally injected carboplatin (CB) 125 mg/kg to produce severe myelosuppression. Mice were then subcutaneously injected with LBP (50, 100, and 200 mg/kg) daily from day 0 to day 6.

The following lab values were obtained from blood samples that were collected from the tail veins of mice at different time points: peripheral white blood cells (WBC), red blood cells (RBC), and platelet (PLT) counts. For the in vitro experiment, researchers incubated human PBMCs with LBP at different concentrations in combination with phytohemagglutinin (PHA), and the production of granulocyte colony-stimulating factor (G-CSF) was tested. Results showed that 50 mg/kg of LBP (LBP-L) significantly ameliorated the decrease of peripheral WBC in irradiated myelosuppressive mice on day 13, and 100 mg/kg LBP (LBP-M) did the same on days 17 and 21. The decrease of peripheral RBC of irradiated myelosuppressive mice was significantly ameliorated by all dosages of LBP on days 17 and 25. LBP-H (200 mg/kg LBP) and LBP-M significantly enhanced peripheral PLT counts of irradiated myelosuppressive mice on days 10, 13, 17, and 21, as did LBP-L on days 13 and 17. WBC counts of chemotherapy-induced myelosuppressive mice were increased by all dosages of LBP to some extent, but there was no statistical difference when compared to the control. On days 13, 15, 17, and 20, LBP-H significantly ameliorated the decrease of peripheral RBC of chemotherapy-induced myelosuppressive mice, and LBP-M and LBP-L did the same on days 15 and 17. On days 7 and 10, peripheral PLT counts of chemotherapy-induced myelosuppressive mice were significantly enhanced by all dosages of LBP, as well as on days 13, 15, and 17 by LBP-H and by LBP-M on days 13 and 15. The authors stated that “LBP could obviously stimulate human PBMCs to produce G-CSF” and concluded that LBP promoted the recovery of peripheral blood of irradiation or chemotherapy-induced myelosuppressive mice and that these effects may be the result of the stimulation of PBMCs to produce G-CSF.

- The therapeutic effects of *Lycium barbarum* polysaccharide (LBP) on mitomycin C (MMC)-induced myelosuppressive mice was investigated (Hai-Yang et al., 2004). After two days of intravenous injections with MMC 150 mg/kg to produce severe myelosuppression, mice were treated by subcutaneous injections of LBP (100 or 200 mg/kg daily) from days 0 to 6. Results showed that LBP significantly ameliorated the decrease in peripheral RBCs, hemoglobin, and hematocrit in myelosuppressive mice. LBP also enhanced peripheral platelet recovery and enhanced mean platelet volume. However, LBP did not affect MMC-induced neutropenia.
- **Hepatic effects:** Researchers reported on the case of a 61 year-old Chinese woman who was stabilized on warfarin and developed an elevated international normalized ratio (INR) after drinking a concentrated Chinese herbal tea (Lam et al., 2001). In addition, they investigated the effect of the tea on CYP2C9, the isoenzyme responsible for the metabolism of S-warfarin. The patient developed an elevated INR of 4.1, with no reported changes in her other medications or lifestyle, except for drinking a concentrated Chinese herbal tea made from *Lycium barbarum* L. fruits (3–4 glasses daily) for four days prior to her clinic visit. After discontinuing the tea, withholding warfarin for one day, and lowering the weekly dose, the follow-up INR seven days later was 2.4, and seven subsequent INR values were in the 2.0–2.5 range. Subsequent in vitro assessment showed a weak inhibition of S-warfarin metabolism by CYP2C9 from the tea of

L. barbarum L., suggesting that the observed interaction may be caused by factors other than the CYP450 system. The authors concluded that there is a potential herbal-drug interaction between warfarin and *L. barbarum* L., and that this herb-drug combination should be avoided.

- **Hepatoprotection effects:** When incubated with two cerebrosides isolated from *Lycium chinense* fruits (1-O-beta-D-glucopyranosyl-(2S, 3R,4E,8Z)-2-N-palmitoyloctadecasphinga-4,8-dienine+ ++ (1) and 1-O-beta-D-glucopyranosyl-(2S,3R,4E,8Z)-2-N-(2'-hydroxypalmitoyl) octadecasphinga-4,8-dienine (2)), there was a significant reduction in the release of glutamic pyruvic transaminase (GPT) and sorbitol dehydrogenase (SDH) from CCl₄-intoxicated hepatocytes (Kim et al., 1997a).
- Researchers investigated the effect of zeaxanthin dipalmitate, a hepatoprotective component of *Lycium chinense*, against carbon tetrachloride-induced hepatotoxicity in rat hepatic parenchymal and nonparenchymal cells in vitro (Kim et al., 1997b). Results showed that cellular malondialdehyde (MDA) levels declined significantly with zeaxanthin treatment in a concentration-dependent manner. Zeaxanthin dipalmitate also inhibited Ito cell proliferation, significantly inhibited collagen synthesis in Ito cells by 65.1% ($p < .05$), and inhibited NO formation in Kupffer cells. These results demonstrate that zeaxanthin dipalmitate exerts a potent hepatoprotective effect.
- Researchers investigated a new cerebroside, LCC, isolated from the fruits of *Lycium chinense* for its hepatoprotective activity in cultured rat hepatocytes exposed to galactosamine (GalN) (Kim et al., 2000). Treatment of these GalN-injured primary cultures with LCC over in concentrations ranging from 1 mcM to 10 mcM markedly blocked the release of both glutamic pyruvic transaminase (GPT) and sorbitol dehydrogenase (SDH) in a dose-dependent manner. Mechanisms of action for the hepatoprotective activity of LCC included significantly restoring the incorporation of [(3)H]-uridine into RNA in a dose-dependent manner and blocking the suppression of RNA synthesis caused by actinomycin D in a dose-dependent manner.
- Researchers investigated the mechanisms by which a novel cerebroside (1-O-(beta-D-glucopyranosyl)-(2S,3R,4E,8Z)-2-N-palmitoyl octadecasphinga-4,8-diene; LCC) from the fruits of *Lycium chinense* Mill. (Solanaceae) exerts its hepatoprotective activity (Kim et al., 1999). Treatment with LCC maintained levels of total and reduced hepatic mitochondrial glutathione (GSH) in cells injured by the hepatotoxicant CCl₄. LCC also significantly increased the activities of glutathione reductase and glutathione peroxidase in CCl₄-injured rat hepatocytes and reduced the elevated levels of MDA seen in CCl₄-injured rat hepatocytes. The authors proposed that LCC may preserve the hepatic mitochondrial level of GSH by scavenging reactive oxygen species produced during CCl₄-induced toxicity. As a result, lipid peroxidation and cellular damage may be reduced.
- Researchers isolated three hepatoprotective compounds (pyrrole derivatives) from fruits of *Lycium chinense* (Chin et al., 2003). At the concentration of 0.1 mcM, two of the compounds showed hepatoprotective effects comparable to silybin.

- Ha et al. investigated the hepatoprotective effect of *Lycium chinense* Miller (Solanaceae) fruit (LFE) against CCl₄-induced hepatotoxicity in rats, as well as the mechanism underlying these protective effects (Ha et al., 2005). Pretreatment with LFE resulted in a significant protective effect by lowering the serum aspartate and alanine aminotransferase (AST and ALT) and alkaline phosphatase (ALP). A histological observation confirmed this hepatoprotective action. Pretreatment with LFE also (1) prevented the elevation of hepatic malondialdehyde (MDA) formation and the depletion of reduced glutathione (GSH) content and catalase activity in the liver of CCl₄-injected rats and (2) decreased the expression of cytochrome P450 2E1 (CYP2E1) mRNA and protein compared with the livers of control group rats. LFE displayed hydroxide radical-scavenging activity in a dose-dependent manner in vitro. These results suggest that the hepatoprotective effects of LFE might be related to antioxidative activity and expressional regulation of CYP2E1.
- **Hepatoprotection effects (hepatic fibrosis):** Researchers investigated the effect of zeaxanthin dipalmitate (ZD), a carotenoid from *Lycium chinense* fruit, on bile duct ligation scission (BDL)-induced hepatic fibrosis in rats (Kim et al., 2002). Results showed that treatment of BDL rats with ZD at a dose of 25 mg/kg of body weight significantly reduced the following parameters: the activities of aspartate transaminase ($p < .05$) and alkaline phosphatase ($p < .001$) in serum, collagen deposition ($p < .01$), levels of thiobarbituric acid reactive substances, and 4-hydroxyproline levels. Therefore, ZD effectively inhibited hepatic fibrosis in BDL rats, at least in part via its antioxidative activity.
- **Hypolipidemic effects:** *Lycium barbarum* fruit water decoction, crude polysaccharide extracts (crude LBP), and purified polysaccharide fractions (LBP-X) were investigated in alloxan-induced diabetic or hyperlipidemic rabbits for their hypoglycemic and hypolipidemic effects (Luo et al., 2004). Data were obtained by measuring blood glucose and serum lipid parameters in sequential trials. Results after 10 days of treatment showed that the three *Lycium barbarum* fruit extracts or fractions significantly reduced blood glucose levels, as well as serum total cholesterol (TC) and triglyceride (TG) concentrations, while simultaneously markedly increasing high-density lipoprotein cholesterol (HDL-c) levels. LBP-X showed a more significant hypoglycemic effect than that of the water decoction and crude LBP, but its hypolipidemic effect seemed to be weaker. These crude extracts were identified as being rich in antioxidants (e.g., carotenoids, riboflavin, ascorbic acid, thiamine, or nicotinic acid). The authors stated that several monosaccharides and 17 amino acids are the major bioactive constituents producing the hypoglycemic effect of *Lycium barbarum* polysaccharides (glycoconjugates). Possible active principles for the hypolipidemic effect are both polysaccharides and vitamin antioxidants from *Lycium barbarum* fruits.
- **Immunologic effects:** In human research, results from available randomized controlled trials suggest that wolfberry alters immune response, such as enhancing the capacity to respond to antigenic challenge (Vidal et al., 2012) and increasing the number of lymphocytes and levels of interleukin-2 and immunoglobulin G (Amagase et al., 2009; Vidal et al., 2012).
- The effects of pure *Lycium barbarum* polysaccharides (LBP-X) on immunological activity were compared with crude LBP in mice (Luo et al., 1999). The pure

LBP-X was divided into different doses. Lower doses in the range of 5–20 mg/kg of pure LBP-X daily showed a remarkable effect on immunological enhancement. At 10 mg/kg daily, LBPX showed a highly significant difference compared with crude LBP on immune indices in mice. The authors concluded that the correct dose of *Lycium barbarum* polysaccharides is necessary to achieve the best pharmacological effect.

- Lbp2, a glycoconjugate isolated and purified from the fruit of *Lycium barbarum* L., was shown to increase rate of phagocytic action and phagocytic index, promote lymphocyte translation and accelerate the production of serum hemolysin (Peng et al., 2001). Lbp2 also effectively scavenged the superoxide anion produced by the DMSO-NaOH system.
- Xu et al. reported on advances in immunopharmacological studies of *Lycium barbarum* L. (Xu, He, Xu, & Liu, 2000).
- **Immunomodulation effects:** Researchers investigated the structures and immunomodulation activity of four homogeneous polysaccharides, LBP 1a-1, LBP 1a-2, LBP 3a-1, and LBP 3a-2, that were isolated from *Lycium barbarum* L., which was brought from Zhongning County, Ningxia Province (Duan et al., 2001). Polysaccharides with a main chain of alpha-(1→4)-D-polygalacturonans (LBP 3a-1 and LBP 3a-2) showed stronger immunomodulation activity than alpha-(1→6)-D-glucans (LBP 1a-1 and LBP 1a-2). All four polysaccharides enhanced splenocyte proliferation induced by ConA.
- The immunomodulatory effects of a polysaccharide-protein complex from *Lycium barbarum* (LBP3p) on the immune system was investigated in S180-bearing mice (Gan et al., 2004). After inoculation with S180 cell suspension, mice were treated orally with LBP3p (5, 10, and 20 mg/kg) for 10 days. Results showed that LBP3p significantly inhibited the growth of transplantable sarcoma S180 and increased the following parameters: macrophage phagocytosis, the form of antibody secreted by spleen cells, spleen lymphocyte proliferation, CTL activity, and IL-2 mRNA expression level. In addition, lipid peroxidation in S180-bearing mice was reduced. These effects were not dose-dependent in a linear fashion. The 10 mg/kg dose was the most effective of the three doses studies.
- Researchers investigated the effects of *Lycium barbarum* polysaccharide-protein complex (LBP(3p)) on the expression of interleukin-2 and tumor necrosis factor-alpha in human peripheral blood mononuclear cells (Gan et al., 2003). In the transcription polymerase chain reaction (RT-PCR) and bioassay, administration of LBP(3p) increased the expression of interleukin-2 and tumor necrosis factor-alpha at both mRNA and protein levels in a dose-dependent manner. The authors proposed that LBP(3p) may induce immune responses and possess potential therapeutic efficacy in cancer.
- **Immunopharmacological effects:** Xu et al. reported on advances in the immunopharmacological study of *Lycium barbarum* L. (Xu et al., 2000).
- **Immunostimulation effects:** The immunoactivity of *Lycium barbarum* glycopeptide (LBG) was investigated in a routinely prepared murine splenic lymphocyte suspension (Du et al., 2004). Four groups were created: a blank control group in the absence of *Lycium barbarum* glycopeptide or ConA, a positive control group in the presence of 0.5 ml of ConA (but in the absence of LBG), a group of four different concentrations of LBG, and a group of four different concentrations

of LBG in combination with 0.5 ml of ConA (10 mcg/ml) added into each well to observe the synergic effects of LBG and ConA as LBG+ConA groups. The samples were incubated for 72 hr at 37°C, then analyzed by CFSE-labeled cells combined with flow cytometry, and MTT. Results showed that LBG could enhance the murine splenic lymphocyte proliferative reaction and that combined use of LBG and ConA had synergic effects. The immunomodulatory effects of yam-boxthorn noodle, a newly developed functional noodle, were investigated in female BALB/c mice after continuously consuming a test diet for five weeks (Lin et al., 2006). Researchers measured the changes in visceral organ weight, immunoglobulin (Ig) A, IgE, IgG, and IgM serum levels, and IgA levels in the intestinal lavage fluid. There was no significant change in body weights and absolute and relative organ weights (lung, heart, liver, spleen, and kidney) compared to those from the control group. When the yam-boxthorn noodle concentration in the AIN 76 diet rose from 3% to 30%, the serum IgA and IgG levels in the experimental group increased significantly. There was no significant change in the IgE and IgM level in the serum, nor in the IgA level in the intestinal lavage fluid. These results suggest that yam-boxthorn noodle in sufficient dietary concentrations may increase serum antibody levels of IgA and IgG in vivo.

- **Infertility effects:** Researchers systematically investigated the effect of *L. barbarum* polysaccharides (LBP) on male infertility in a rat model of testis damage induced by a physical factor (43°C heat exposure), on DNA damage of mouse testicular cells induced by a chemical factor (H₂O₂), and on sexual behavior and reproductive function of hemicastrated male rats (Luo et al., 2006). The results showed that LBP had a positive and protective effect on all studied parameters, including a protective effect against the testicular tissue damage induced by heat exposure, a significant increase in testis and epididymis weights, improved superoxide dismutase (SOD) activity, and raised sexual hormone levels in the damaged rat testes. LBP also protected against DNA oxidative damage of mouse testicular cells induced by H₂O₂ in a dose-dependent manner. In hemicastrated male rats, LBP improved the copulatory performance and reproductive function, such as shortened penis erection latency and mount latency, regulated secretion of sexual hormones, increased hormone levels, raised accessory sexual organ weights, and improved sperm quantity and quality. These results provide scientific evidence to support the traditional use of *L. barbarum* fruits as an aphrodisiac and a traditional remedy for male infertility in China.
- **Macular degeneration effects:** One of the richest natural sources of the carotenoid zeaxanthin is wolfberry (fructus *Lycium barbarum* L.; Gou Qi Zi and Kei Tze) (Benzie et al., 2006). Zeaxanthin is concentrated in the macula and has been reported to protect against age-related macular degeneration, but the bioavailability of carotenoids is low. In human subjects, the bioavailability of zeaxanthin from wolfberry was significantly (three-fold) higher from a hot milk formulation ($p < .001$) than from warm milk or water formulations. In other human research, Lacto-Wolfberry (a proprietary milk-based formulation of goji) prevented the hypopigmentation and soft drusen accumulation in the macula that occurred in the placebo group (Bucheli et al., 2011). Plasma zeaxanthin levels and total antioxidant capacity both increased.

- Zeaxanthin is an oxygenated carotenoid that has antioxidant and blue light-absorbing properties. It accumulates in the macula, where it may help to prevent age-related macular degeneration (Cheng et al., 2005). Researchers investigated the effect of dietary supplementation with whole wolfberries on fasting plasma zeaxanthin concentration in a single-blinded, placebo-controlled human intervention trial of parallel design. Fasting blood was collected from healthy, consenting subjects. Fourteen subjects took 15 g of wolfberry (estimated to contain almost 3 mg zeaxanthin) daily for 28 days. Repeat fasting blood was collected on day 29. Thirteen age- and sex-matched controls took no wolfberry. Plasma zeaxanthin levels increased 2.5-fold between day 1 and day 29 in the supplementation group ($p < .01$), indicating that zeaxanthin in whole wolfberries is bioavailable, and that plasma zeaxanthin levels will increase markedly with intake of a modest daily amount.
- Plasma zeaxanthin concentrations increased significantly ($p = .05$) after volunteers consumed a 5 mg dose suspended in yogurt together with a balanced breakfast (Breithaupt et al., 2004). Peak absorption occurred between 9 and 24 hr. Native 3R,3'R-zeaxanthin from wolfberry was determined to be more bioavailable than the nonesterified form, based on a two-sided F and t -test of the respective areas under the curve ($p = .05$).
- **MAO inhibition effects:** MAO-A and MAO-B are two subtypes of monoamine oxidase (MAO), the enzyme that catalyzes the oxidative deamination of biogenic amines (Lin et al., 2003). The regulation of MAO-B has particular importance in treating neurodegenerative diseases. Researchers investigated the inhibitory effect of 27 species of plants used in traditional Chinese medicine on MAO-B in rat brain homogenates. The best activity and selectivity toward MAO-B (with IC_{50} values of 0.44, 0.29, 0.40, and 0.03 mg/ml, respectively) was exhibited by the 50% aqueous extracts of *Arisaema amurense*, *Lilium brownii* var. *colchesteri*, *Lycium chinense*, and *Uncaria rhynchophylla*. The authors suggested that these extracts may be useful in delaying the progressive degeneration caused by neurological diseases.
- **Neuroprotective effects:** Researchers investigated the neuroprotective effects of *Lycium barbarum* extract against toxins in rat cortical neurons exposed to fibrillar Abeta (1–42) and Abeta (25–35) (Yu et al., 2005). While control neurons exposed to Abeta peptides experienced apoptosis and necrosis, pretreatment with *L. barbarum* extract significantly reduced the release of lactate dehydrogenase (LDH), as well as attenuating Abeta peptide-activated caspases-3-like activity. *L. barbarum* extract demonstrated a wider range of therapeutic dose than that of a well-known western neuroprotective medicine lithium chloride (LiCl). Pretreatment with the aqueous extract markedly reduced the Abeta peptides induced phosphorylation of JNK-1 (Thr183/Tyr185) and its substrates c-Jun-I (Ser 73) and c-Jun-II (Ser 63). These results demonstrate the neuroprotective effects of an extract from *L. barbarum* and may be a therapeutic option for the prevention of Alzheimer's disease.
- **Pancreatic effects:** Researchers studied the effects of *Lycium barbarum* polysaccharide (LBP) on alloxan-induced isolated islet cells damage in rat islet cells in vitro (Xu, Zhang, & Wang, 2002). LBP inhibited the alloxan-induced significant

decrease in SOD activity and increase in MDA production, demonstrating protective effects on alloxan-induced isolated rat islet cell damage.

- **Periodontal effects:** Researchers investigated the effects of *Lycium barbarum* L. and *Drynaria fortunei* J. Smith on in vitro attachment and growth of human gingival fibroblasts to root surfaces (Liu, 1992). At a dose of 1.25 mg/ml, both herbs improved attachment and growth of fibroblasts on the planed diseased root surfaces to a certain extent. *Lycium barbarum* had more potent effects. When exposed to this herb, cells on the diseased root surfaces increased markedly in number, with more even distribution, better spread, and more exuberant growth. The results suggest that these two herbs may be effective in improving the formation of new attachment of periodontal tissue.
- **Pulmonary effects:** Betaine, coumarin, hesperidin, and kaempferol, components derived from *Lycium chinense*, *Angelicae decursiva*, *Poncirus trifoliata*, and *Polygonatum odoratum*, respectively, were investigated for their effects on mucin release in cultured hamster tracheal surface epithelial cells (Lee et al., 2004). In this study, the possible activities of these agents were compared to the inhibitory action on mucin release by poly-L-lysine and the stimulatory action by adenosine triphosphate. After metabolically radio-labeling confluent primary hamster tracheal surface epithelial cells, they were treated for 30 min in the presence of varying concentrations of each agent to assess the effects on (3)H-mucin release. Results showed that coumarin and kaempferol did not affect mucin release significantly, while betaine and hesperidin increased mucin release at the highest concentration. The authors concluded that betaine and hesperidin may increase mucin release by directly acting on airway mucin-secreting cells, and they suggested that these agents deserve further research on their possible use as mild expectorants in the treatment of chronic airway diseases.
- **Radioprotective effects:** Intraperitoneal injection of crude extracts from *Lycium chinense* root (LCR) and *Lycium chinense* aerial part (LCA) for seven days before whole-body X-irradiation prevented bone marrow death in ICR strain mice (Hsu et al., 1999). In the irradiation range of 4–8Gy, various treatments enhanced endogenous hematopoietic spleen colony formation (CFUs). The extract of LCR at a dose of 500 mg/kg significantly stimulated the recovery of leukocyte, erythrocyte, and thrombocyte counts and stimulated recovery of the hematocrit. These effects were not observed at the 250 mg/kg dose. The radioprotective action may be induced by a possible process of enhanced regeneration of the hematopoietic stem cells as a result of enhanced postirradiation repair or increased proliferation of the hematopoietic stem cells.
- **Radiosensitizing effects:** The radiosensitizing effects of the *Lycium barbarum* polysaccharide (LBP) were observed by the model transplanted Lewis lung cancer on C57 BL mice (Lu & Cheng, 1991). *Lycium barbarum* polysaccharide (LBP) administered alone to Lewis lung cancer transplanted C57 BL mice did not inhibit lung cancer growth. However, the combination of LBP and radiation demonstrated significant radiosensitizing effects; the mean numerical value of the dose-modifying factors (DMF) was 2.05. The results also showed certain radiation enhancement to acute hypoxic cells of Lewis lung cancer. Little toxicity to the mice was observed with administration of LBP.

- **Skin protective effects:** Due to its antioxidant and antiapoptotic properties, researchers investigated the effects of *Lycium barbarum* L. (Solanaceae) glycoconjugates (LbGp) in full-thickness human skin and in dermal fibroblasts (Zhao et al., 2005). Results showed that LbGp significantly decreased the level of MMP (matrix metalloproteinase)-1 but did not decrease MMP-3 or -13 in the whole human skin system. The viability of the skin was not compromised. LbGp also inhibited MMP-1-dependent skin expansion under mechanical stress. The researchers found that one of glycoconjugates, LbGp5, promoted the survival of human fibroblasts cultured in suboptimal conditions. In addition, these cultures also contained higher levels of the MMP-1 substrate-collagen type I in the presence of LbGp5. The authors suggested that *L. barbarum* glycoconjugates in general and LbGp5 in particular may have important skin-protective properties.
- **Weight loss effects:** In human research, *L. barbarum* increased VO_2 and affected metabolic rate and energy expenditure in a dose-dependent manner (Amagase & Nance, 2011).

Pharmacodynamics/Kinetics

- **Absorption:** One of the richest natural sources of the carotenoid zeaxanthin is wolfberry (fructus *Lycium barbarum* L.; Gou Qi Zi and Kei Tze) (Benzie et al., 2006). Zeaxanthin has been reported to protect against age-related macular degeneration. Since the bioavailability of carotenoids is low, researchers investigated three preparations of wolfberry to ascertain the bioavailability of zeaxanthin from wolfberries in human subjects. Berries were homogenized in three different liquids: hot (80°C) water, warm (40°C) skimmed milk, and hot (80°C) skimmed milk, each subsequently freeze-dried into a powder. In a crossover trial, 12 healthy subjects randomly consumed a standardized 15 mg dose of zeaxanthin from each preparation daily with a standardized breakfast. There was a —three-to-five-week washout period between treatments. Blood samples were taken at baseline and 2, 4, 6, 7, 8, and 10 hr after ingesting zeaxanthin. For all formulations, zeaxanthin levels in the triacylglycerol-rich lipoprotein fraction of plasma peaked at 6 hr after ingestion. The bioavailability of zeaxanthin was significantly (three-fold) higher from the hot milk formulation ($p < .001$) than from the warm milk and water formulations. In human research, consumption of Lacto-Wolfberry increased plasma zeaxanthin levels (Bucheli et al., 2011).
- Plasma zeaxanthin concentrations increased significantly ($p = .05$) after volunteers consumed a 5 mg dose suspended in yogurt together with a balanced breakfast (Breithaupt et al., 2004). Peak absorption occurred between 9 and 24 hr. Native 3R,3'R-zeaxanthin from wolfberry was determined to be more bioavailable than the nonesterified form, based on a two-sided *F* and *t*-test of the respective areas under the curve ($p = .05$).
- Researchers investigated the effect of dietary supplementation with whole wolfberries on fasting plasma zeaxanthin concentration in a single-blind, placebo-controlled human intervention trial of parallel design (Cheng et al., 2005; Sin et al., 2013). Fasting blood was collected from healthy, consenting subjects; 14 subjects took 15 g of wolfberry daily for 28 days (estimated to contain almost 3 mg of zeaxanthin). Repeat fasting blood was collected on day 29. Thirteen age- and

sex-matched controls took no wolfberry. Plasma zeaxanthin levels increased 2.5-fold between day 1 and day 29 in the supplementation group, ($p < .01$) indicating that zeaxanthin in whole wolfberries is bioavailable and that plasma zeaxanthin levels will increase markedly with intake of a modest daily amount.

HISTORY

- According to secondary sources, goji berry appears in Chinese lore as far back as 2800 BC in association with the legendary First Emperor, Shen Nung, who was an herbalist and the mythical father of agriculture. In addition to the Mandarin Chinese name *gouqi* (which is the source of the name *goji*), Japan, Korea, Vietnam, Thailand, and Tibet all have names for goji in their native languages. Approximately 70 species of *Lycium* grow in separate and distinct regions distributed in temperate to subtropical parts of North America, South America, southern Africa, Eurasia, and Australia. The original habitat of goji is not known. *Lycium* spp. are part of the Solanaceae family, which includes tomatoes, potatoes, eggplants, and peppers, as well as the toxic herbs tobacco and deadly nightshade.
- According to secondary sources, China is the main supplier of commercially grown wolfberries worldwide. In the 21st Century, goji berries and juice have become increasingly popular “superfoods” in the Western world. Exports from China to the United States in 2004 were valued at \$120 million. According to secondary sources, some of the “organic” goji berry products sold in the United States may not meet U.S. or Canadian organic standards, as official organic certification processes are lacking in the parts of Asia where wolfberries are commercially grown.

EVIDENCE TABLE

Condition Treated	Study Type	Author, Year	N	Statistically Significant Results?	Quality of Study: 0-2 = poor 3-4 = good 5 = excellent	Magnitude of Benefit (how strong is the effect?)	Absolute Risk Reduction	# of Patients Needed to Treat for One Outcome	Comments
Cancer	Randomized controlled trial	Cao, 1994	79	Yes	1	Small	24.8%	4	LAK/IL-2 with and without <i>Lyctium barbarum</i> polysaccharides (LBP).
Cognition	Randomized controlled trial	Amagase, 2009	60	Yes	3	Small	NA	NA	Small changes in general well-being and some immune measures compared to placebo.
Immunomodulation	Randomized controlled trial	Amagase, 2009	60	Yes	3	Small	NA	NA	Small changes in general well-being and some immune measures compared to placebo.
Vision	Randomized controlled trial	Amagase, 2009	60	No	3	NA	NA	NA	Lack of effect on vision in healthy adults.
Weight loss/obesity	Randomized controlled trial	Amagase, 2011	33	Mixed	3	NA to large (waist reduction)	NA	NA	Decreased waist circumference with lack of effect on body weight.
Well-being	Meta-analysis	Hsu, 2012	Four trials	Mixed	NA	NA to small	NA	NA	Meta-analysis of four of the authors' own studies.
Well-being	Randomized controlled trial	Amagase, 2008	35	Yes	4	Small	NA	NA	Endpoints were mainly subjective.
Well-being	Randomized controlled trial	Amagase, 2009	60	Yes	3	Small	NA	NA	Small changes in general well-being and some immune measures compared to placebo.
Well-being	Randomized controlled trial	Amagase, 2008	P	P	P	P	P	P	P

Explanation of Columns in Natural Standard Evidence Table

1	2	3	4	5	6	7	8	9	10
Condition	Study design	Author, N year		Statistically significant?	Quality of study 0-2 = poor 3-4 = good 5 = excellent	Magnitude of benefit	Absolute risk reduction	Number needed to treat	Comments

Condition

- Refers to the medical condition or disease targeted by a therapy.

Study Design

Common types include:

- **Randomized controlled trial (RCT):** An experimental trial in which participants are assigned randomly to receive either an intervention being tested or placebo. Note that Natural Standard defines RCTs as being placebo-controlled, while studies using active controls are classified as equivalence trials (see below). In RCTs, participants and researchers are often blinded (i.e., unaware of group assignments), although unblinded and quasi-blinded RCTs are also often performed. True random allocation to trial arms, proper blinding, and sufficient sample size are the basis for an adequate RCT.
- **Equivalence trial:** An RCT that compares two active agents. Equivalence trials often compare new treatments to usual (standard) care, and may not include a placebo arm.
- **Before and after comparison:** A study that reports only the change in outcome in each group of a study, and does not report between-group comparisons. This is a common error in studies that claim to be RCTs.
- **Case series:** A description of a group of patients with a condition, treatment, or outcome (e.g., 20 patients with migraine headache underwent acupuncture and 17 reported feeling better afterwards). Case series are considered weak evidence of efficacy.
- **Case-control study:** A study in which patients with a certain outcome are selected and compared to similar patients (without the outcome) to see if certain risk factors/predictors are more common in patients with that outcome. This study design is not common in the complementary and alternative medicine literature.
- **Cohort study:** A study which assembles a group of patients with certain baseline characteristics (e.g., use of a drug), and follows them forward in time for outcomes. This study design is not common in the complementary and alternative medicine literature.
- **Meta-analysis:** A pooling of multiple trials to increase statistical power (often used to pool data from a number of RCTs with small sample sizes, none which

demonstrates significance alone but in aggregate can achieve significance). Multiple difficulties are encountered when designing/reviewing these analyses; in particular, outcomes measures or therapies may differ from study to study, hindering direct comparison.

- Review: An author's description of his or her opinion based on personal, non-systematic review of the evidence.
- Systematic review: A review conducted according to pre-specified criteria in an attempt to limit bias from the investigators. Systematic reviews often include a meta-analysis of data from the included studies.

Author, Year

- Identifies the study being described in a row of the table.

N

- The total number of subjects included in a study (treatment group plus placebo group). Some studies recruit a larger number of subjects initially, but do not use them all because they do not meet the study's entry criteria. In this case, it is the second, smaller number that qualifies as *N*. *N* includes all subjects that are part of a study at the start date, even if they drop out, are lost to follow-up, or are deemed unsuitable for analysis by the authors. Trials with a large number of dropouts that are not included in the analysis are considered to be weaker evidence for efficacy. For systematic reviews, the number of studies included is reported. For meta-analyses, the number of total subjects included in the analysis or the number of studies may be reported.

Statistically Significant?

- Results are noted as being statistically significant if a study's authors report statistical significance, or if quantitative evidence of significance is present (such as *p* values). *P* = pending verification.

Quality of Study

- A numerical score between 0 –and 5 is assigned as a rough measure of study design/reporting quality (0 being weakest and 5 being strongest). This number is based on a well-established, validated scale developed by Jadad et al. (Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Controlled Clinical Trials* 1996;17[1]:1–12). This calculation does not account for all study elements that may be used to assess quality (other aspects of study design/reporting are addressed in the “Evidence Discussion” sections of reviews).
- A Jadad score is calculated using the seven items in the table below. The first five items are indications of good quality, and each counts as one point toward an overall quality score. The final two items indicate poor quality, and a point is subtracted for each if its criteria are met. The range of possible scores is 0 to 5.

Jadad Score Calculation

Item	Score
Was the study described as randomized (this includes words such as randomly, random, and randomization)?	0/1
Was the method used to generate the sequence of randomization described and appropriate (table of random numbers, computer-generated, etc.)?	0/1
Was the study described as double blind?	0/1
Was the method of double blinding described and appropriate (identical placebo, active placebo, dummy, etc.)?	0/1
Was there a description of withdrawals and dropouts?	0/1
Deduct one point if the method used to generate the sequence of randomization was described and it was inappropriate (patients were allocated alternately, or according to date of birth, hospital number, etc.).	0/-1
Deduct one point if the study was described as double blind but the method of blinding was inappropriate (e.g., comparison of tablet vs. injection with no double dummy).	0/-1

Magnitude of Benefit

- This summarizes how strong a benefit is: small, medium, large, or none. If results are not statistically significant “NA” for “not applicable” is entered. In order to be consistent in defining small, medium, and large benefits across different studies and reviews, Natural Standard defines the magnitude of benefit in terms of the standard deviation (SD) of the outcome measure. Specifically, the benefit is considered:
 - Large: if >1 SD
 - Medium: if 0.5 to 0.9 SD
 - Small: if 0.2 to 0.4 SD
- In many cases, studies do not report the standard deviation of change of the outcome measure. However, the change in the standard deviation of the outcome measure (also known as effect size) can be calculated, and is derived by subtracting the mean (or mean difference) in the placebo/control group from the mean (or mean difference) in the treatment group, and dividing that quantity by the pooled standard deviation (Effect size = [Mean Treatment – Mean Placebo]/SDp).

Absolute Risk Reduction

- This describes the difference between the percent of people in the control/placebo group experiencing a specific outcome (control event rate), and the percent of people in the experimental/therapy group experiencing that same outcome (experimental event rate). Mathematically, Absolute risk reduction (ARR) equals experimental event rate minus control event rate. ARR is better able to discriminate between large and small treatment effects than relative risk reduction (RRR), a calculation that is often cited in studies ([control event rate – experimental event rate]/control event rate). Many studies do not include adequate data to calculate the ARR, in which cases “NA” is entered into this column. *P* = pending verification.

Number Needed to Treat

- This is the number of patients who would need to use the therapy under investigation, for the period of time described in the study, in order for one person to experience the specified benefit. It is calculated by dividing the Absolute Risk Reduction into 1 (1/ARR). *P* = pending verification.

Comments

- When appropriate, this brief section may comment on design flaws (inadequately described subjects, lack of blinding, brief follow-up, not intention-to treat, etc.), notable study design elements (crossover, etc.), dosing, and/or specifics of study group/subgroups (age, gender, etc.). More detailed description of studies is found in the “Evidence Discussion” section that follows the “Evidence Table” in Natural Standard reviews.

EVIDENCE DISCUSSION

Asthma

- **Summary:** In asthma patients, the traditional Chinese medicine (TCM) concoction “Invigorating Kidney,” which includes wolfberry together with six other herbs, improved the maximal expiratory flow-volume curve (MEFV). This research does not provide any data about wolfberry specifically, but it is worthwhile for its contribution to the scientific literature on traditional Chinese herbalism. Further research is needed to determine the effect of wolfberry.
- **Select combination study (not included in the Evidence Table):** Fu et al. reported on a case series that investigated the therapeutic effect of “Invigorating Kidney,” a Chinese herbal decoction, in 35 asthmatic patients in the convalescent stage (Fu, 1989). These 35 patients were chosen from a larger group of 66 asthmatics after measurement of maximal expiratory flow-volume curve (MEFV) revealed abnormal results for FEV, PEF, V75, V50, and V25 compared to healthy persons. These results indicated the presence of airway obstruction (primarily small airways) in these individuals. “Invigorating Kidney” formula was administered in the following daily dosage for 10 weeks: *Viscum coloratum* 15 g, *Psoralea corylifolia* 15 g, *Eucommia ulmoides* 15 g, *Lycium chinense* 9 g, *Tussilago farfara* 15 g, *Artemisia capillaris* 9 g, and *Pogostemon cablin* 9 g. Results showed that various parameters of MEFV “improved to some extent,” indicating that it is possible to reverse airway obstruction in convalescing asthmatics with this Chinese herbal formula.

Cancer

- **Summary:** Polysaccharide constituents, such as the alpha- and beta-glucans from a variety of plants, are reported to have immune system-enhancing properties. In this human clinical trial, *Lycium barbarum* polysaccharides (LBP) demonstrated a synergistic effect in the treatment of various cancers, when administered in conjunction with powerful immune-stimulating drugs. This study provides the first human data to support the existing in vitro and animal research (Liu et al.,

2000; Lu & Cheng, 1991) that establishes the immune-boosting effects of LBP. Further research on wolfberry alone is needed.

- **Evidence (polysaccharides):** Cao et al. conducted a randomized controlled trial with 79 advanced cancer patients to assess the therapeutic effect of *Lycium barbarum* polysaccharides (LBP) vs. LBP combined with LAK/IL-2 (lymphokine-activated killer cells) vs. LAK/IL-2 only (Cao et al., 1994). All patients included in the trial were diagnosed with malignant tumors that were unresponsive to conventional therapy and had stopped treatment for at least one month. Exclusion criteria included severe cardiac, pulmonary, hepatic, and renal illnesses; hypersensitivity to biological products; and pregnancy or lactation. Patients were randomly divided into two groups: one group started taking oral LBP four weeks prior to initiating LAK/IL-2 treatment, and the other group took placebo four weeks prior to LAK/IL-2 treatment. LBP was dosed at 1.7 mg/kg of body weight daily. Standardization of LBP was not discussed. Both groups were given LBP until the termination of the study, which ran from February 1992 to November 1993. Seventy-five patients were available for evaluation of the initial treatment results. The response rate of patients treated with the combination therapy was 40.9% versus 16.1% in the LAK/IL-2 group ($p < .05$). There was a lack of an intent-to-treat analysis. Those who could not complete the study or follow up before November 1, 1993, were not included in the final analysis. Withdrawals were not discussed. The method of randomization was unclear, and the presence of blinding could not be confirmed. The combination treatment resulted in a greater increase in NK and LAK cell activity, as well as a significantly longer “mean remission.” Researchers observed objective regression of cancers in patients with malignant melanoma, renal cell carcinoma, colorectal carcinoma, lung cancer, nasopharyngeal carcinoma, and malignant hydrothorax. They concluded that LBP “may be used as an adjuvant in the biotherapy of cancer.”

Cognition

- **Summary:** Results from available human research suggest a lack of effect of goji on cognition in healthy adults (Amagase et al., 2009). Further research is needed.
- **Evidence:** Amagase et al. conducted a randomized, double-blind, placebo-controlled trial to assess the benefits of *Lycium barbarum* on immune function, visual function, cognitive function, and general well-being ($N = 60$) (Amagase et al., 2009). Healthy Chinese individuals aged 55–72 years from Hunan Province, China, were included in the study. All included participants lacked brain, heart, liver, lung, kidney, or blood disease. Participants also lacked a history of long-term medication use or previous exposure to GoChi™. Use of *Lycium barbarum* or foods containing *Lycium barbarum* was prohibited for at least two months prior to and during the study. Participants included in the study were randomized to receive 60 ml of GoChi™ or placebo twice daily (for a total of 120 ml daily) for 30 days. The GoChi™ product was reported to contain an equivalent amount of *Lycium barbarum* polysaccharides as 150 g of fresh fruit. According to the investigators, a lack of treatment-related adverse effects was observed in this study for both the treatment group and the placebo group. According to the investigators, toxic effects were lacking, based on measurements of sleep,

energy, food intake, urine, stool, body weight, pulse rate, and blood pressure. All participants completed the study. The authors of the study reported two recent case reports of an interaction between warfarin and *Lycium barbarum* fruit tea. However, reports of interactions from this particular clinical trial were lacking. Objective outcome measures included visual function, short-term memory and attention, levels of interleukin (IL)-2, IL-4, immunoglobulin G (IgG), and IgA, and the number of CD4, CD8, lymphocytes, and natural killer (NK) cells. Subjective outcome measures included general feelings of well-being, such as fatigue and sleep, as well as a tendency for increased short-term memory and focus based on a questionnaire. Compared to baseline, participants treated with GoChi™ showed a significant improvement in overall well-being (from 4.33 ± 0.31 to 3.00 ± 0.30 , $p < .05$). Compared to the placebo group, which lacked this change, the improvement was statistically significant ($p < .05$). A significantly greater percentage of participants in the GoChi™ group reported improvement in feelings of well-being compared to the placebo group (63.3% vs. 20.0%, respectively, $p < .05$). Significant improvements in visual function or memory and attention were lacking. Compared to baseline, participants treated with GoChi™ showed significant increases in number of lymphocytes (from 1.76 ± 0.05 to $2.23 \pm 0.03 \times 10^6/\text{ml}$, $p < .05$), levels of IL-2 (from 5.94 ± 0.53 to 9.36 ± 0.60 , $p < 0.05$), and levels of IgG (from 14.12 ± 0.52 to 16.78 ± 0.50 , $p < .05$). Compared to the placebo group, which lacked these changes, these three increases were statistically significant ($p < .05$). However, treatment with GoChi™ lacked a significant effect on the percentages of CD4, CD8, and NK cells, as well as levels of IL-4 and IgA. The study was limited by the lack of detailed description of compliance in participants that completed the study. Also, details regarding the methods of randomization and blinding were unclear.

Immunomodulation

- **Summary:** Results from available randomized controlled trials suggest that wolfberry alters immune response, such as enhancing the capacity to respond to antigenic challenge (Vidal et al., 2012) and increasing the number of lymphocytes and levels of interleukin-2 and immunoglobulin G (Amagase et al., 2009). However, some endpoints in these studies were negative. Further research is required with appropriate primary endpoints.
- **Evidence:** Amagase et al. conducted a randomized, double-blind, placebo-controlled trial to assess the benefits of *Lycium barbarum* on immune function, visual function, cognitive function, and general well-being ($N = 60$) (Amagase et al., 2009). Healthy Chinese individuals aged 55–72 years from Hunan Province, China, were included in the study. All included participants lacked brain, heart, liver, lung, kidney, or blood disease. Participants also lacked a history of long-term medication use or previous exposure to GoChi™. Use of *Lycium barbarum* or foods containing *Lycium barbarum* was prohibited for at least two months prior to and during the study. Participants included in the study were randomized to receive 60 ml of GoChi™ or placebo twice daily (for a total of 120 ml daily) for 30 days. The GoChi™ product was reported to contain an equivalent amount of *Lycium barbarum* polysaccharides as 150 g of fresh fruit. According

to the investigators, a lack of treatment-related adverse effects was observed in this study for both the treatment group and the placebo group. According to the investigators, toxic effects were lacking, based on measurements of sleep, energy, food intake, urine, stool, body weight, pulse rate, and blood pressure. All participants completed the study. The authors of the study reported two recent case reports of an interaction between warfarin and *Lycium barbarum* fruit tea. However, reports of interaction from this particular clinical trial were lacking. Objective outcome measures included visual function, short-term memory and attention, levels of interleukin (IL)-2, IL-4, immunoglobulin G (IgG), and IgA, and the number of CD4, CD8, lymphocytes, and natural killer (NK) cells. Subjective outcome measures included general feelings of well-being, such as fatigue and sleep, as well as a tendency for increased short-term memory and focus based on a questionnaire. Compared to baseline, participants treated with GoChi™ showed a significant improvement in overall well-being (from 4.33 ± 0.31 to 3.00 ± 0.30 , $p < .05$). Compared to the placebo group, which lacked this change, the improvement was statistically significant ($p < .05$). A significantly greater percentage of participants in the GoChi™ group reported improvement in feelings of well-being compared to the placebo group (63.3% vs. 20.0%, respectively, $p < .05$). Significant improvements in visual function or memory and attention were lacking. Compared to baseline, participants treated with GoChi™ showed significant increases in number of lymphocytes (from 1.76 ± 0.05 to $2.23 \pm 0.03 \times 10^6/\text{ml}$, $p < .05$), levels of IL-2 (from 5.94 ± 0.53 to 9.36 ± 0.60 , $p < .05$), and levels of IgG (from 14.12 ± 0.52 to 16.78 ± 0.50 , $p < .05$). Compared to the placebo group, which lacked these changes, these three increases were statistically significant ($p < .05$). However, treatment with GoChi™ lacked a significant effect on the percentages of CD4, CD8, and NK cells, as well as levels of IL-4 and IgA. The study was limited by the lack of detailed description of compliance in participants that completed the study. Also, details regarding the methods of randomization and blinding were unclear.

- **Select combination study (not included in the Evidence Table):** Vidal et al. conducted a randomized, double-blind, placebo-controlled trial to assess the immunomodulatory effects of Lacto-Wolfberry supplementation in the elderly ($N = 150$) (Vidal et al., 2012). Healthy Chinese men and women aged 65–70 years who were attending the XuShe Community Day Care Center for Elderly Persons were included in the trial. Participants were excluded if they were experiencing deteriorating health or rapid weight loss; had a terminal or chronic disease; presented with an immunodeficiency disease, allergy, or lactose intolerance; had been vaccinated within 15 days of the study; had participated in another clinical trial within three months of the study; or used medications that influenced the immune system. Participants were randomized by a computer-generated randomization list to receive 13.7 g of Lacto-Wolfberry formulation or placebo. Both products were dissolved in 200 ml of hot water or soup at lunchtime. Treatment was administered daily for 92 days. Each gram of Lacto-Wolfberry product contained 530 mg of wolfberry fruit, 290 mg of bovine skimmed milk, and 180 mg of maltodextrin. Each gram of placebo product consisted of 290 mg of bovine skimmed milk, 200 mg of maltodextrin, 476 mg of sucrose, and 34 mg of colorants. Serious adverse effects were lacking. However, vomiting and fever occurred in

the Lacto-Wolfberry group. Significant changes indicative of toxic effects, including changes in body weight, blood pressure, pulse rate, or blood biochemistry, were lacking for both groups during the study. Of the randomized participants, 10 from the treatment group and 7 from the placebo group withdrew from the study prior to completion. The investigators reported that reasons for withdrawals were unrelated to the study, but further details were lacking. Information on interactions was lacking. Outcome measures included antibody response to an influenza vaccine, in vivo T cell-mediated immune response, and inflammatory status. Compared to the placebo group, participants who received the Lacto-Wolfberry intervention showed a significant increase in total IgG levels 60 days postvaccination (11.25 vs. 11.58 g/L, respectively $p = .0075$) and 90 days postvaccination (11.96 vs. 13.92 g/L, respectively, $p < .0001$), as well as influenza-specific IgG levels at 60 (estimated ratio (ER) = 1.49, 95% CI: 1.18–1.88, $p = .0011$) and 90 days (ER = 1.67, 95% CI: 1.23–2.27, $p = .0012$). A statistically significant change in IgM was lacking ($p = .9669$). Between days 30 and 90, participants treated with Lacto-Wolfberry showed a significantly improved seroconversion rate compared to the placebo group (27.7% vs. 8.8%, respectively, OR = 3.4, 95% CI: 1.21–9.61, $p = .021$). Compared to the placebo group after 90 days, the Lacto-Wolfberry group lacked a significant increase in positive rate postvaccination ($p = .092$). Statistically significant between-group differences in autoantibodies (antithyroglobulin and anti-DNA antibodies) and T-cell function were lacking based on in vivo analysis. Also, significant differences in inflammatory markers, albumin, or prealbumin were lacking between the two groups. Limitations of this study included a small inclusion population and narrow spectrum of generalizability.

Skin Aging

- **Summary:** In vitro, a combination of Himalayan actives including goji berries attenuated ultraviolet B (UVB)-induced cell apoptosis of skin organ epidermis and decreased TNF-alpha secretion (Wineman et al., 2012). In human research, topical application reduced wrinkle depth (Wineman et al., 2012). The effect of goji berries alone is not clear, and further research is needed.
- Wineman et al. conducted a study to examine the effect of a product containing a combination of Himalayan actives including goji berries on skin wrinkle depth and skin moisture (Wineman et al., 2012). Topical application resulted in a reduction in wrinkle depth and an increase in skin moisture. The effect of goji berries alone is not clear.

Vision

- **Summary:** Goji is popularly marketed as a dietary supplement for vision enhancement in single and combination products. Goji berry has a high concentration of nutrients, including vitamins A, C, and E, and carotenoids, beta-carotene, lutein, and zeaxanthin (Benzie et al., 2006). Zeaxanthin is an oxygenated carotenoid that accumulates in the macula, where it may help to prevent age-related macular degeneration (Benzie et al., 2006; Cheng et al., 2005; Weller & Breithaupt, 2003). Preliminary research has found that zeaxanthin in whole wolfberries is

bioavailable, and that plasma zeaxanthin levels will increase markedly with intake of a modest daily amount (Breithaupt et al., 2004; Cheng et al., 2005; Sin et al., 2013). In vivo animal reports have demonstrated the therapeutic function of *Lycium barbarum* against neurodegeneration in the retina of rats, and thus this extract may be a potential candidate for the development of neuroprotective drug against the loss of retinal ganglion cells in glaucoma (Chang & So, 2007). A combination product was found to improve xerophthalmia in postmenopausal women (Wei et al., 2009). However, human studies are lacking, and high-quality research is needed to confirm the efficacy of goji for vision enhancement or prevention of vision disorders.

- **Evidence:** Amagase et al. conducted a randomized, double-blind, placebo-controlled trial to assess the benefits of *Lycium barbarum* on immune function, visual function, cognitive function, and general well-being ($N = 60$) (Amagase et al., 2009). Healthy Chinese individuals aged 55–72 years from Hunan Province, China, were included in the study. All included participants lacked brain, heart, liver, lung, kidney, or blood disease. Participants also lacked a history of long-term medication use or previous exposure to GoChi™. Use of *Lycium barbarum* or foods containing *Lycium barbarum* was prohibited for at least two months prior to and during the study. Participants included in the study were randomized to receive 60 ml of GoChi™ or placebo twice daily (for a total of 120 ml daily) for 30 days. The GoChi™ product was reported to contain an equivalent amount of *Lycium barbarum* polysaccharides as 150 g of fresh fruit. According to the investigators, a lack of treatment-related adverse effects was observed in this study for both the treatment group and the placebo group. According to the investigators, toxic effects were lacking, based on measurements of sleep, energy, food intake, urine, stool, body weight, pulse rate, and blood pressure. All participants completed the study. The authors of the study reported two recent case reports of an interaction between warfarin and *Lycium barbarum* fruit tea. However, reports of interaction from this particular clinical trial were lacking. Objective outcome measures included visual function, short-term memory and attention, levels of interleukin (IL)-2, IL-4, immunoglobulin G (IgG), and IgA, and the number of CD4, CD8, lymphocytes, and natural killer (NK) cells. Subjective outcome measures included general feelings of well-being, such as fatigue and sleep, as well as a tendency for increased short-term memory and focus based on a questionnaire. Compared to baseline, participants treated with GoChi™ showed a significant improvement in overall well-being (from 4.33 ± 0.31 to 3.00 ± 0.30 , $p < .05$). Compared to the placebo group, which lacked this change, the improvement was statistically significant ($p < .05$). A significantly greater percentage of participants in the GoChi™ group reported improvement in feelings of well-being compared to the placebo group (63.3% vs. 20.0%, respectively, $p < .05$). Significant improvements in visual function or memory and attention were lacking. Compared to baseline, participants treated with GoChi™ showed significant increases in number of lymphocytes (from 1.76 ± 0.05 to $2.23 \pm 0.03 \times 10^6/\text{ml}$, $p < .05$), levels of IL-2 (from 5.94 ± 0.53 to 9.36 ± 0.60 , $p < .05$), and levels of IgG (from 14.12 ± 0.52 to 16.78 ± 0.50 , $p < .05$). Compared to the placebo group, which lacked these changes, these three increases were statistically significant ($p < .05$). However, treatment with GoChi™ lacked a significant effect on

the percentages of CD4, CD8, and NK cells, as well as levels of IL-4 and IgA. The study was limited by the lack of detailed description of compliance in participants that completed the study. Also, details regarding the methods of randomization and blinding were unclear.

- **Systematic review (not included in Evidence Table):** Sin et al. conducted a systematic review to assess the effects of lifestyle modifications, diet, and use of nutritional supplements and vitamins for preventing or treating age-related macular degeneration (AMD) (Sin et al., 2013). The effects of smoking, weight loss, omega-3 fatty acids, lutein, vitamin B, vitamin C, vitamin E, *Ginkgo biloba*, beta-carotene, zinc, copper, black currant, and blueberries were assessed in this review but are excluded from this summary focusing on *Lycium barbarum* L. (also known as wolfberry and fructus *Lycii*). One included study assessed the effects of *Lycium barbarum* on plasma zeaxanthin (an examination of clinical effects was lacking) (Cheng et al., 2005). Relevant studies published in English up to December 2010 were pooled from MEDLINE, PubMed, the Cochrane Library, and Google Scholar. Meta-analyses, cohort studies, and case-controlled studies were included in the review. Studies were excluded if they were case series, case reports, abstracts, reports of personal observations, or commentaries. Participants in the included study were administered whole wolfberries. Information regarding treatment duration was lacking. The wolfberries were reported to contain zeaxanthin (zeaxanthin dipalmitate), but details regarding standardization was lacking. Information regarding allergies, adverse events, toxic effects, dropouts, and interactions was also lacking. Outcome measures included changes in plasma levels of zeaxanthin. According to the reviewers, the included study showed that the ingestion of whole wolfberries resulted in significantly increased fasting levels of zeaxanthin in the plasma. This review was limited by the inclusion of only one study relevant to wolfberries. Additional research is needed before conclusion may be made regarding the benefits of wolfberries in patients with AMD.
- **Select combination study (not included in the Evidence Table):** Wei et al. conducted a study to examine the effect of Runmushu Oral Liquid for the treatment of xerophthalmia in postmenopausal women ($N = 72$) (Wei et al., 2009). Patients were treated with Hialid eyedrops alone or in combination with Runmushu Oral Liquid (rehmannia root, figwort, lilyturf root, dendrobium stem, wolfberry fruit, chrysanthemum, and sticktight) for one month. Endpoints included subjective and objective indices. The total effective rate was 86.1% (62/72) in the treatment group versus 66.7% (48/72) in the control group ($p < .01$) after one month. Other significant improvements included improvements in subjective symptom scores ($p < .01$), tear film breakup time, and Schirmer I test ($p < .01$). Significant differences in cornea fluorescein staining scores were lacking between groups. The effect of wolfberry fruit alone is not clear from this study.
- Bucheli et al. conducted a randomized, double-blind, placebo-controlled trial to determine the effect of Lacto-Wolfberry (a proprietary milk-based formulation of goji) on pigmentation and soft drusen count in the macula, as well as plasma antioxidant capacity, in elderly subjects ($N = 150$) (Bucheli et al., 2011). The patients received 13.7 g of Lacto-Wolfberry or placebo daily for 90 days. Reported adverse effects were lacking. Endpoints included pigmentation, soft drusen count in the macula, plasma zeaxanthin, and total antioxidant capacity. Plasma

zeaxanthin levels increased by 26% in the wolfberry group, and the total antioxidant capacity increased by 57%. Also, although there was demonstrated hypopigmentation and soft drusen accumulation in the macula in the placebo group, this was lacking in the wolfberry group. The effect of wolfberry alone is not clear from this study.

Weight Loss/Obesity

- **Summary:** In a clinical trial of GoChi™ fruit juice, the juice resulted in an increased reduction in waist circumference, but not a reduction in body weight, in subjects that were also exercising (Amagase & Nance, 2011). Well-designed studies with appropriate randomization are needed to confirm these results.
- **Evidence:** Amagase and Nance conducted two randomized, double-blind, placebo controlled, studies to assess the effects of *L. barbarum* on the expenditure of calories ($N = 8$) and changes in waist circumference ($N = 33$) (Amagase & Nance, 2011). In both studies, healthy individuals aged at least 18 years were included. Participants were excluded from either study if they presented with heart, hepatic, lung, or renal disease; if they were allergic to *L. barbarum* or other similar juices, if they were taking anticoagulant agents such as warfarin; if they had acute or chronic conditions (medical or psychiatric); or if they were pregnant or breastfeeding. During the run-in period and throughout the study, participants were required to avoid using dietary supplements, energy drinks, caffeine-containing beverages, green tea, or foods that contained *L. barbarum*. Both studies were preceded by a two-week run-in period. During the first study, participants were randomized to receive a nutritional beverage (Boost Plus, Nestle Healthcare Nutrition Inc., Minneapolis, MN) plus 120 ml of juice containing 0 ml (placebo) 30 ml, 60 ml, or 20 ml of *L. barbarum* juice. Following a one-week washout period, participants were crossed over to other treatment groups, until all participants had consumed each treatment twice. During the second study, participants consumed 120 ml of *L. barbarum* or placebo daily (90 ml at breakfast and 30 ml at bedtime) for 14 days. Participants in both groups of the second study also exercised and followed a diet. The *L. barbarum* fruit juice (GoChi™, FreeLife International Inc., Phoenix, AZ) was prepared from *L. barbarum* fruit. The yield from the fresh plant was approximately 35%, and the juice contained *L. barbarum* polysaccharides (LBP) that were equivalent to those found in 150 g of fresh fruit. Information regarding allergies, adverse effects, and toxic effects was lacking. Information regarding dropouts was lacking for the first study. During the second study, four participants dropped out ($N = 2$ from each group) due to personal reasons. Information regarding interactions was lacking for both studies. In the first study, outcome measures included changes in resting metabolic rate (RMR) and postprandial energy expenditure (PPEE), which were assessed based on changes in breath oxygen volume (VO_2). In the second study, outcome measures included waist circumference, body weight, body mass index (BMI), and total body fat. During the first study, participants treated with 120 ml of *L. barbarum* showed statistically significant increased VO_2 after 1 hr compared to the placebo group (56.26 ± 5.72 ml/min vs. 24.58 ± 4.04 ml/min, respectively, $p < .05$). Also, participants who consumed 120 ml of *L. barbarum* showed significantly increased levels of VO_2 compared to baseline after 4 hr ($p < .05$),

while the VO_2 levels for all other groups had returned to the baseline level. Also, participants who consumed 120 ml of *L. barbarum* showed significantly greater area under the curve of VO_2 compared to the placebo group (32.19 ± 3.01 L vs. 10.42 ± 4.09 L, $p < .05$). This between-group difference was lacking for the other two treatment groups. The investigators concluded that *L. barbarum* affected metabolic rate and energy expenditure in a dose-dependent manner. During the second study, participants in the *L. barbarum* group showed a reduction in waist circumference of 5.54 ± 0.65 cm by day 15, while participants in the placebo group showed a reduction of 0.88 ± 0.83 cm. Statistically significant changes in body weight, BMI, and total body fat was lacking for both groups. The investigators concluded that treatment with *L. barbarum* significantly reduced waist circumference when used in combination with diet and exercise. Limitations of both of these studies included lack of information regarding the methods of randomization and blinding. In addition, it is unclear whether all participants randomized in the first study completed the trial. Also, the number of participants included in the second study was lower than the number needed to assess the efficacy of *L. barbarum* with 95% confidence and 80% power.

Well-being

- **Summary:** Hsu et al. conducted a meta-analysis of to examine the effects of *Lycium barbarum* on general well-being; however, only four of the author's own studies were found (Paul Hsu et al., 2012). One study appeared to have been included in the meta-analysis, although endpoints related to well-being were lacking (the study was focused on weight loss and energy expenditure) (Amagase & Nance, 2011). According to the results of this meta-analysis and the included studies, at least one brand of *Lycium barbarum*, GoChi™, appears to improve some measures of well-being. Further research is required by other groups and using other brands of goji.
- **Meta-analysis:** Hsu et al. conducted a meta-analysis of four randomized, blinded, placebo-controlled studies (Amagase, Sun, & Nance, 2008; Amagase & Nance, 2008; Amagase & Nance, 2011; Amagase et al., 2009) to assess the effects of *Lycium barbarum* on general well-being ($N = 161$) (Paul Hsu et al., 2012). The reviewers searched MEDLINE for relevant articles published until April 2011. However, the reviewers reported that they were unable to find any relevant articles using this search, so they conducted a meta-analysis of results from four of their own previously published studies. In all included studies, participants consumed 120 ml of *L. barbarum* (GoChi™, FreeLife International, Phoenix, AZ) daily for 14–30 days. Information regarding standardization, allergies, adverse effects, and toxic effects was lacking. According to the reviewers, several dropouts occurred from both groups in most of the studies. Reasons for dropouts included missing treatments for multiple days, relocation, and other personal issues. Information regarding interactions was lacking. Outcome measures included participant assessment of 46 items related to physical and psychological fatigue, gastrointestinal issues, musculoskeletal issues, and cardiovascular issues. Compared with the placebo group, participants treated with GoChi™ showed significant improvements in weakness (SMD = 0.59, 95% CI: 0.12–1.07, $p = .0145$), stress (SMD = 0.57, 95% CI: 0.17–0.97, $p = 0.005$), mental acuity (SMD = 0.51, 95%

CI: 0.07–0.94, $p = .0216$), ease of awakening (SMD = 0.57, 95% CI: 0.14–0.99, $p = .0088$), shortness of breath (SMD = 0.47, 95% CI: 0.07–0.86, $p = .0219$), focus on activity (SMD = 0.61, 95% CI: 0.04–1.18, $p = .0347$), sleep quality (SMD = 0.58, 95% CI: 0.17–0.98, $p = .0050$), daydreaming (SMD = 0.73, 95% CI: 0.22–1.25, $p = .0054$), and overall feelings of health and well-being (SMD = 0.63, 95% CI: 0.23–1.03, $p = .0021$), based on a random-effects model. Based on a fixed-effects model, participants treated with GoChi™ also showed additional improvements in calmness (SMD = 0.61, 95% CI: 0.09–1.13, $p = .0205$), fatigue (SMD = 0.53, 95% CI: 0.13–0.94, $p = .0103$), depression (SMD = 0.45, 95% CI: 0.05–0.85, $p = .0287$), and circulation (SMD = 0.40, 95% CI: 0.00–0.80, $p = .0486$) compared to the placebo group. Between-group differences regarding the remaining items on the questionnaire were lacking. Based on a random-effects model, the odds ratio indicated a significantly higher chance of improving fatigue (OR = 3.51, 95% CI: 1.45–8.48, $p = .0054$), dizziness (OR = 2.65, 95% CI: 1.15–6.12, $p = .0224$), and sleep quality (OR = 3.23, 95% CI: 1.23–8.47, $p = .0169$) following treatment with GoChi™ vs. placebo. This meta-analysis was limited by the fact that all of the included studies were conducted by the authors of the meta-analysis. In addition, financial support for the meta-analysis was provided by the manufacturers and marketers of GoChi™ juice.

- Evidence:** Amagase and Nance conducted a randomized, double-blind, placebo-controlled study to assess the effects of *Lycium barbarum* (goji) on general health ($N = 35$) (Amagase & Nance, 2008). Healthy individuals aged at least 18 years were included in the study. Participants were excluded if they presented with heart, liver, lung, or kidney disease; if they were allergic to *L. barbarum* or similar fruit juices; if they were receiving treatment for liver, kidney, or immune disorders; if they were using the anticoagulant Coumadin®; or if they had other serious medical or psychiatric conditions. Following a two-week washout period, participants were randomized to receive 120 ml of GoChi™ or placebo once daily in the morning for 14 days. Each 120 ml serving of GoChi™ contained the amount of *Lycium barbarum* polysaccharides found in approximately 150 g of fresh fruit. According to the investigators, reports of adverse effects were lacking during the study. Information regarding toxic effects was lacking. One participant in the treatment group was excluded after missing treatment doses for several days. All participants in the placebo group completed the study. Information regarding interactions was lacking. Outcome measures included height, body weight, body mass index (BMI), systolic and diastolic blood pressure, body fat, total water content of the body, pulse rate, eye fatigue, overall vision, and overall well-being based on a questionnaire consisting of 30 symptoms related to physical and psychological fatigue. Compared to baseline and the placebo group, treatment with GoChi™ lacked a statistically significant effect on height, body weight, BMI, systolic and diastolic blood pressure, body fat, total water content of the body, pulse rate, eye fatigue, and overall vision. However, compared to baseline, treatment with GoChi™ resulted in a statistically significant improvement in fatigue (from 1.63 ± 0.407 to 0.81 ± 0.245 , $p = .017$), athletic performance (from 2.20 ± 0.380 to 0.94 ± 0.249 , $p = .025$), stress (from 2.00 ± 0.329 to 1.38 ± 0.352 , $p = .037$), quality of sleep (from 2.07 ± 0.403 to 0.56 ± 0.241 , $p = .002$), ease of awakening (from 2.06 ± 0.370 to 0.87 ± 0.291 , $p = .023$), calmness (from

2.63 ± 0.386 to 0.94 ± 0.232, $p = .005$), focus when doing activities (from 2.69 ± 0.472 to 1.00 ± 0.224, $p = .009$), feeling healthy (from 2.25 ± 0.359 to 0.81 ± 0.209, $p = .006$), feeling content (from 2.19 ± 0.400 to 0.80 ± 0.296, $p = 0.025$), feeling happy (from 2.38 ± 0.455 to 0.88 ± 0.328, $p = .023$), and bowel regularity (from 2.00 ± 0.516 to 0.69 ± 0.299, $p = .037$). Compared to baseline, participants in the placebo group showed a significant improvement in feeling happy (from 1.72 ± 3.86 to 0.78 ± 0.263, $p = .015$) and heartburn (from 0.72 ± 0.311 to 0.11 ± 0.076, $p = .028$). Limitations of this study included lack of information regarding the method of randomization. Also, most of the outcome measures were based on subjective rather than objective measurements, and between-group comparisons were lacking.

- Amagase et al. conducted a randomized, double-blind, placebo-controlled trial to assess the benefits of *Lycium barbarum* on immune function, visual function, cognitive function, and general well-being ($N = 60$) (Amagase et al., 2009). Healthy Chinese individuals aged 55–72 years from Hunan Province, China, were included in the study. All included participants lacked brain, heart, liver, lung, kidney, or blood disease. Participants also lacked a history of long-term medication use or previous exposure to GoChi™. Use of *Lycium barbarum* or foods containing *Lycium barbarum* was prohibited for at least two months prior to and during the study. Participants included in the study were randomized to receive 60 ml of GoChi™ or placebo twice daily (for a total of 120 ml daily) for 30 days. The GoChi™ product was reported to contain an equivalent amount of *Lycium barbarum* polysaccharides as 150 g of fresh fruit. According to the investigators, a lack of treatment-related adverse effects was observed in this study for both the treatment group and the placebo group. According to the investigators, toxic effects were lacking, based on measurements of sleep, energy, food intake, urine, stool, body weight, pulse rate, and blood pressure. All participants completed the study. The authors of the study reported two recent case reports of an interaction between warfarin and *Lycium barbarum* fruit tea. However, reports of interaction from this particular clinical trial were lacking. Objective outcome measures included visual function, short-term memory and attention, levels of interleukin (IL)-2, IL-4, immunoglobulin G (IgG), and IgA, and the number of CD4, CD8, lymphocytes, and natural killer (NK) cells. Subjective outcome measures included general feelings of well-being, such as fatigue and sleep, as well as a tendency for increased short-term memory and focus based on a questionnaire. Compared to baseline, participants treated with GoChi™ showed a significant improvement in overall well-being (from 4.33 ± 0.31 to 3.00 ± 0.30, $p < .05$). Compared to the placebo group, which lacked this change, the improvement was statistically significant ($p < .05$). A significantly greater percentage of participants in the GoChi™ group reported improvement in feelings of well-being compared to the placebo group (63.3% vs. 20.0%, respectively, $p < .05$). Significant improvements in visual function or memory and attention were lacking. Compared to baseline, participants treated with GoChi™ showed significant increases in number of lymphocytes (from 1.76 ± 0.05 to 2.23 ± 0.03 × 10⁶/ml, $p < .05$), levels of IL-2 (from 5.94 ± 0.53 to 9.36 ± 0.60, $p < .05$), and levels of IgG (from 14.12 ± 0.52 to 16.78 ± 0.50, $p < .05$). Compared to the placebo group, which lacked these changes, these three increases were statistically significant

($p < .05$). However, treatment with GoChi™ lacked a significant effect on the percentages of CD4, CD8, and NK cells, as well as levels of IL-4 and IgA. The study was limited by the lack of detailed description of compliance in participants that completed the study. Also, details regarding the methods of randomization and blinding were unclear.

- Amagase et al. conducted a randomized controlled trial to examine the effect of a *Lycium barbarum* fruit juice on general well-being (Amagase et al., 2008). Further information is pending.

BRANDS USED IN CLINICAL TRIALS/THIRD-PARTY TESTING

- GoChi™ (FreeLife International, Phoenix, AZ) (Amagase et al., 2008; Amagase & Nance, 2008; Amagase & Nance, 2011; Amagase et al., 2009; Paul Hsu et al., 2012).
- Kei Tze, Gou Qi Zi (Benzie et al., 2006; Cheng et al., 2005).

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